Banbury Center cold spring harbor laboratory 2003 COLD SPRING HARBOR

BANBURY CENTER

Banbury Center is a 50-acre estate adjoining the waters of Long Island Sound on the north shore of Long Island, barely 40 miles east of downtown Manhattan and some five miles from Cold Spring Harbor Laboratory. The estate was donated to the Laboratory in 1976 by Charles Sammis Robertson together with funds for necessary architectural conversions and an endowment to cover upkeep of the grounds and the original estate structures. With the Laboratory's international reputation for research and education, the magnificent Banbury grounds and buildings are an ideal site for a complementary program of smaller conferences concentrating on aspects of the biological sciences which also bear significant social implications. Banbury's primary interests are in the areas of molecular biology and genetics, especially as they relate to health, social, and policy issues.

What was once the estate's original seven-car garage is now the Conference Center, containing administrative offices, a small library, and—at its center—a conference room of an ideal shape and size for workshop-style discussion meetings. Complete with extensive, unobtrusive sound and projection facilities as well as wall-to-wall blackboard space, the room can accommodate as many as 40 participants while remaining equally conducive to either formal presentations or informal give-and-take.

The Robertsons' family house, situated on the final promontory before the grounds descend to the shore of the harbor, now serves as the center for participant accommodations and dining, while the extensive grounds, swimming pool, tennis court, and beach present ample recreational resources. Onsite accommodations were supplemented by the opening in 1981 of the Sammis Hall guest house—a modern embodiment of the sixteenth century Palladian villas—designed for the Center by the architectural firm of Moore Grover Harper. In 1997, the Meier House, opposite the Conference Center, was added to provide extra housing so that everyone attending a Banbury Center meeting can stay on the estate.



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BANBURY CENTER DIRECTOR'S REPORT

There were 19 meetings at the Banbury Center in 2003, with 654 participants. Of these, 530 (81%) came from the United States, drawn from 33 states. As usual, New York, Maryland, Massachusetts, and California provided most participants (46% of the total), reflecting the many research institutions in those states. Participants from abroad came from 21 countries, once again showing the high esteem in which meetings at Banbury are held throughout the world. The Watson School of Biological Sciences held two week-long "Topics in Biology" courses, and there were five lecture courses in the Laboratory's Meetings and Courses Program. Finally, two local groups made use of the Center. As usual, the program dealt with eclectic, interesting, and often controversial topics. The meetings ranged from discussions of some of the oldest problems in biology, such as What is a species?, through theoretical biology, to biomedical topics of the greatest practical importance for many millions of people. There was also one very special event in 2003—Banbury Center's 25th anniversary.

Our 25th Anniversary

That the Banbury Center exists is due to the foresight and wisdom of Charles Robertson, a pivotal figure in the modern development of Cold Spring Harbor Laboratory. He first made a most generous gift of \$7.5 million in 1973 to establish the Robertson Fund, the major part of the Laboratory's endowment. Two years later, in 1975, Robertson gifted his Lloyd Harbor estate of some 45 acres and the buildings on it to the Laboratory. These included the family house and a large garage, together with an endowment intended to contribute to the upkeep of the buildings and the estate. It is said that Robertson wanted laboratories built on the site, but this was impractical for financial and esthetic reasons. Instead, Jim Watson suggested that the estate be used for small, workshop-style meetings to complement the large meetings held on the main campus.

Robertson agreed and the garage was converted into a spacious seminar room, with large windows on two sides and a high, vaulted ceiling. These features make our Conference Room so unlike the typical seminar room and its ambience contributes significantly to the success of meetings at Banbury. Another striking feature is the chalkboard across the full width of the room. I can remember Jane Gitschier explaining the polymerase chain reaction to science journalists, beginning at the left side of the board and drawing a diagram that took up all 30 feet of the board. The family house-now named Robertson House-was modified to accommodate meetings participants. (Extra accommodation was provided a few years later when funding from the Max C. Fleischmann and Kresge Foundations was used to build Sammis Hall, and many years later the Meier House was purchased.)



The garage prior to renovations.



The garage during renovations.



The garage today as a conference room.



Cocktails during the 25th Anniversary Party.



D. West, P. Travaglianti, B. Stillman, G. Stillman, K. Friedman



H. Varmus, J. Watson

On June 14, 1977, Francis Crick gave a talk at a small dedication ceremony of what was now called the Banbury Center. Victor McElheny was appointed the first director in early 1978 and Charles Robertson's vision for his family's gift to the Laboratory was properly realized when the first meeting was held in May 1978, on Assessing Chemical Mutagens: The Risk to Humans.

We celebrated the Silver Anniversary of that meeting with a small party on September 12. Guests included Bill Robertson and Anne Meier (two of Charles and Marie Robertson's children), former directors Victor McElheny (1978–1982) and Michael Shodell (1982–1986), and friends from Lloyd Harbor. Harold Varmus, Nobel laureate, former director of the National Institutes of Health, and current President of Memorial Sloan-Kettering Cancer Research Center, was the guest of honor. The evening began with cock-

tails in the Conference Room, and was followed by dinner at Robertson House. Dr. Varmus, a frequent participant in Banbury Center meetings, gave a short talk describing the importance of the Banbury Center in promoting biomedical research. It was a delightful evening and made us look forward to what the next 25 years will bring. (In our first 25 years, there were 380 meetings attended by over 11,000 participants.)

Planning and Promoting Biomedical Research

Without exception, all Banbury Center meetings have a significant effect on those participating in them, but there are some meetings that have a demonstrated impact far beyond the confines of the Conference Room. These are fascinating meetings, combining critical reviews of science with discussions of science policy. One example was the 1994 meeting on sequencing the *Arabidopsis* genome that ultimately led to the international effort to complete the sequence. There were similar meetings on three different topics at Banbury in 2003.

L. Joshua-Tor (Cold Spring Harbor Laboratory) and W. Hendrickson (Columbia University) organized the *Scientific Opportunities in Macromolecular Crystallography at NSLS-II* meeting in July. NSLS stands for the National Light Synchrotron Source II that is to be built at Brookhaven National Laboratory. X-ray crystallography is achieving remarkable results in determining the atomic structures of huge molecular complexes. These successes are due to technical advances, not the least of which is the use of very powerful X-rays produced by synchrotrons. This meeting brought together X-ray crystallographers from the relevant institutions to discuss their needs for the NSLS-II. Notable among these was Rod McKinnon, who three months later won the Noble Prize for his work on channel complexes.

We now have the complete sequence of the human genome, but a huge amount of work needs to be done to understand it. A key strategy will be to use other, more tractable experimental animals such as the mouse and the rat. These have different benefits, but the mouse has the edge in terms of its genetics. Mutations are key to doing genetics, and a large number of naturally occurring mouse mutants have been found during the past 100 years. But systematic mutagenesis screens, while expensive and time-consuming to do, have proved invaluable for other organisms, for example, zebrafish. R. Woychik (The Jackson Laboratory) and C. Austin (National Human Genome Research Institute) organized the *Mouse Genome-wide Targeted Mutagenesis* meeting at Banbury to review the scientific and financial issues of carrying out a genome-wide mutagenesis of the mouse. This was an extraordinarily intensive meeting with discussions going on late into the night.

DNA sequence analysis is also being applied to organisms much more esoteric than human and mouse. For many years, taxonomists have used molecular comparisons of proteins and DNA sequences to estimate the relatedness of organisms. Now there is a proposal to use DNA sequences as molecular "bar codes," to use DNA sequences as unique identifiers of species; if a purported new species has the same bar code as one known already, then it is not a new species. The proposal is controversial on scientific grounds—is it right and will it work?—and because it seems to be replacing the skills of the taxonomist with a robotic sequencing machine. The Alfred P. Sloan Foundation funded two meetings to review this proposal. The first meeting, Taxonomy and DNA, was organized by R. De Salle (American Museum of Natural History), S. Federhen (National Library of Medicine, National Institutes of Health), and P. Hebert (University of Guelph, Canada). It reviewed some of the fundamental questions: How well do these molecular approaches conform with current methods for defining species? How can molecular data be integrated with other taxonomic data? What are the practical issues involved in carrying this out on a large scale? The second meeting, Taxonomy, DNA, and the Bar Code of Life, organized by J. Baker (Academy of Natural Sciences, Philadelphia) and J. Hanken (Harvard University) was primarily a planning meeting, focusing on how to proceed with a museum-based, large-scale DNA bar-coding effort, including strategy, policy, funding, and organization. These remarkable meetings have led to the establishment of a "Bar Code of Life Initiative" Consortium to further these plans.

Plant Science

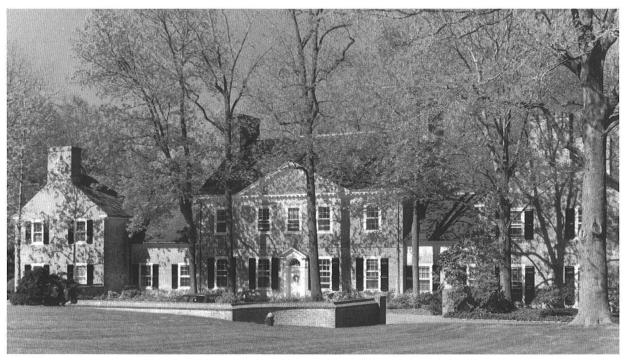
The foundations of developmental biology were laid through observation and experimental manipulation, but now, genomic and comparative genomic approaches are giving us the tools to determine how

limbs or leaves develop. An inflorescence is a cluster of flowers all arising from the same stem, and much work has been done on the genetic basis for inflorescence development in *Arabidopsis*. However, this meeting, *Regulation of Inflorescence Morpholog: Insights from Genetics and Genomics*, organized by E. Kellogg (University of Missouri, St. Louis) and D. Jackson (Cold Spring Harbor Laboratory) and funded by the Cold Spring Harbor Laboratory Corporate Sponsor Program, focused on other plant and nonplant developmental systems. Participants explored how developmental genetics, quantitative trait analysis, and comparative biology can help to discover genes that establish and regulate meristem identity and determine how these gene products interact.

Theoretical Biology

There have been recurring attempts to establish a theoretical biology, in the same way that theoretical physics exists as a well-defined field. These have not been successful—perhaps all kinds of biologists have far too much to discover experimentally to need guidance from theorists. Nevertheless, there are areas where a theoretical approach may well be helpful.

The discussions of species showed how seriously taxonomists take words and descriptions; they aim for unambiguous definitions of a Monarch butterfly or an Indian elephant. Laboratory scientists have been less careful with words and descriptions, using names and concepts that may not have consistent definitions in different research fields. The need for consistency and for new descriptive tools is becoming ever more urgent as the flood of data, and its complexity, continues to increase. The meeting *Formal Languages for Biological Processes*, organized by Y. Lazebnik (Cold Spring Harbor Laboratory), D. Endy (Massachusetts Institute of Technology), and A. Finney (California Institute of Technology) examined some of the approaches being taken to represent biological processes so that they can be more effectively analyzed and understood. Participants were drawn from three areas: experimental biologists who should use these methods, biologists who have successfully used formal approaches, and developers (often mathematicians) of these approaches. The meeting was funded by the Cold Spring Harbor Laboratory Corporate Sponsor Program.



Robertson House provides housing accommodations at Banbury Center.

A second meeting tackling theoretical approaches to biological problems examined some of the simplest gene networks, those of bacteriophage. Organized by S. Adhya (National Cancer Institute), D. Court (National Cancer Institute), and A. Oppenheim (The Hebrew University), *Quantitative Genetic Networks* focused on the quantitative aspects of the genetic and biochemical components underlying the regulatory networks found governing the alternative lifestyles found in bacteriophages. It was remarkable the degree to which even these seemingly simple networks pose problems for formualting theoretical descriptions and devising modern experimental approaches to solve specific complex gene control processes. The meeting was funded by the National Cancer Institute.

Neuroscience

The two Banbury Center meetings on neuroscience also had strong theoretical underpinnings. *Neural Circuits: Principles of Design and Operation* was organized by K.D. Miller (University of California, San Francisco) and H.S. Seung (Massachusetts Institute of Technology). Funded by the Swartz Foundation, the meeting brought together experimentalists and theoreticians working on operation of neuronal circuits. The participants considered results on cortical circuitry, compared and contrasted results from visual, somatosensory, and auditory cortex and the bird song system, and considered theoretical and engineering approaches to the construction of neural circuits.

The second meeting, Neural Representation and Processing of Temporal Patterns, was organized by C. Brody (Cold Spring Harbor Laboratory), D. Buonomano (University of California, Los Angeles), and J. Hawkins (Redwood Neuroscience Institute). Processing of temporal patterns is a fundamental component of sensory and motor function. Given the inherent temporal nature of our interaction with the environment, understanding how the brain processes time is a necessary step toward understanding the brain. Participants considered the following fundamental problems: How is time represented in the brain? How are complex temporal patterns perceived and produced? Participants included psychologists, neuroscientists, and theorists working on these problems, and the meeting was funded by the Redwood Neuroscience Institute.

Human Neurological and Neurodegenerative Disorders

Three meetings dealt with neurological and neurodegenerative disorders. A fourth meeting dealt with stem cells and is included here, given that stem cells may prove to be effective in neurodegenerative diseases.

Banbury has regularly held meetings on Fragile-X syndrome, most recently funded by the FRAXA Research Foundation. Research on Fragile-X is at a most interesting stage, with evidence that abnormalities may exist in the formation of contacts between nerve cells. This is generating a large amount of intense research which was reviewed in the meeting *Synaptic Function in Fragile-X*, organized by M. Bear (Brown University) and M. R. Tranfaglia (FRAXA Research Foundation). It focused on the biological activity of the FMRP protein and on its role in dendrite formation. Most importantly, understanding the mechanisms involved will lead to identifying other components which may be therapeutic targets.

Research on amyotrophic lateral sclerosis (ALS)—the most common form of motor neuron diseases—is also at a most interesting stage. From 5% to 10% of ALS is inherited, and in 20% of these families, there are mutations in the enzyme Cu/Zn Superoxide dismutase 1. This discovery made a major impact on the field, but the mechanism of SOD1 toxicity remains unclear and the cause(s) of the remaining ALS cases is unknown. These latter cases were the subject of *Finding New Genes Linked to Amyotrophic Lateral Sclerosis: A Focus on Current Technologies and Their Potential Application*, organized by R. Brown (Massachusetts General Hospital) and L. Bruijn (The ALS Association) and funded by the ALS Association. It examined how the complete human genome sequence and new technology advances can be used to look for the genetic components of these unknown cases. The discovery of new genes, either linked to familial disease or susceptibility genes in the sporadic cases, is critical for a better understanding of the disease and the potential for new therapeutic targets.

Banbury Center held a meeting on schizophrenia for the first time since the early 1990s. Since then, several areas of the genome have been suspected of harboring genes contributing to schizophrenia, but no gene has yet been pinned down. On the other hand, there have been advances in the neuropharmacology of schizophrenia, particularly in the role of a molecule called NMDA. Participants in this meeting, *Integrating Progress in the Genetics and Neuropharmacology of Schizophrenia*, organized by R. Cloninger (Washington University) and J. Coyle (Harvard University), attempted to bring together both areas of research. The goals of the meeting were to identify new technical and experimental advances in the fields of genetics, cognitive development, brain imaging, and neuropharmacology that might be applied to understanding schizophrenia. The meeting was funded by the Cold Spring Harbor Laboratory Corporate Sponsor Program.

No area of contemporary biomedical research has been more controversial than studies of human stem cells. The promise of using stem cells for therapy is great, but much still must be learned about the biology of these remarkable cells. R. McKay (National Institute of Neurological Disorders and Stroke) organized a meeting, *Controlling the Differentiation of Pluripotent Cells*, that examined how these cells differentiate into many cell types, and the ways in which this differentiation might be directed. A key question is the extent to which work on other organisms, in particular the mouse, can be extrapolated to human cells. The ethical implications of this work were not ignored; there was an energetic discussion of some of the philosophical underpinnings of people's reactions to human stem cell research. The meeting was funded by the Cold Spring Harbor Laboratory Corporate Sponsor Program.

Cancer

The meetings on cancer in 2003 all concentrated on clinical issues, rather than on research on the fundamental causes of cancer.

Two meetings dealt with very interesting forms of cancer. The first was on *The Biology of Neuroendocrine Tumors*, organized by A. Levine (Institute for Advanced Studies), and E. Vosburgh (Verto Institute), and funded by the Verto Institute. These carcinoid and other neuroendocrine tumors are derived from cells that share neural and endocrine features. They have a unique biology that determines the clinical features of the tumors and that might be exploited in developing treatments. These treatments might be very different from those currently available for other cancers. This meeting provided an opportunity to bring together current and future Verto investigators, and the Scientific Advisors of the Verto Institute.

The second meeting dealt with a related group of unusual cancers, pheochromocytomas, which secrete catecholamines and cause hypertension. *Molecular Differentiation of Benign and Malignant Pheochromocytomas and Neuroblastomas*, organized by G. Eisenhofer (National Institutes of Health), W.M. Manger (National Hypertension Association, Inc.), and R.M. Weinshilboum (Mayo Foundation), was funded by the National Hypertension Association, Inc. There are no reliable prognostic markers to assess whether a pheochromocytoma will metastasize—presumably these differences in behavior reflect the underlying mutations and differences in expression of genes regulating cellular growth and survival. An understanding of these pathways of gene expression should therefore allow identification of molecular markers of malignancy and possible new targets for therapeutic intervention. Participants reviewed current methods for distinguishing benign from malignant forms of pheochromocytoma and went on to survey the use of microarrays and other genomics-based tools for detecting malignancy in these types of tumor.

Finally, T. Kreiner (Affymetrix, Inc.), T. Golub (Whitehead Institute for Biomedical Research), and D. Dalma-Weiszhausz (Affymetrix, Inc.) organized a meeting, *Taking Cancer Genomics to the Clinic*, funded by Affymetrix, Inc. This was a high-level discussion workshop that examined how genomic approaches to cancer will promote the implementation of new techniques and strategies. In particular, participants reviewed the current diagnostic and prognostic clinical practices in the treatment of cancer and how techniques such as microarrays might change them. Participants included cancer researchers, clinicians, policy-makers, and members of advocacy groups, and an important goal of the meeting was to strengthen the relationships in the cancer world among advocacy groups, researchers, policy-makers, the FDA, and technology providers.

Infectious Diseases and Chronic Disorders

Toward a More Unified Understanding of Infectious Disease, organized by V. McGovern (Burroughs Wellcome Fund) and S. James (The Ellison Medical Foundation), and funded by the Burroughs Wellcome Fund, reviewed the current state of basic research in the human pathogens. After surveying the impact and potential of genomic and postgenomic approaches, participants went on to consider where infectious diseases research is going, and how a more comprehensive understanding of the interface between pathogens and host can be gained. One goal of the meeting was to explore the desirability of integrating research across the pathogens, and the difficulties involved in taking this broader approach. It is a sign of the times that veterinary pathogens were included in the discussions.

Infectious pathogens were also part of the meeting *Toward Understanding the Cellular and Molecular Mechanisms of Medically Unexplained Fatigue*. This topic is highly controversial precisely because it is medically unexplained and so, in the view of many, such fatigue does not exist except in the mind of the individual. For this reason, the organizers, W.C. Reeves and S.D. Vernon (Centers for Disease Control & Prevention) and C. Heim (Emory University), covered a remarkably wide range of topics, from infections and toxins, to how the mind influences onset and recovery. Funded by the Centers for Disease Control & Prevention, it was a thought-provoking meeting that included discussions of mind/body relationships.

Vaccines

Banbury Center has hosted a series of colloquia sponsored by the Albert B. Sabin Vaccine Institute on key issues limiting the production and distribution of vaccines, particularly to the most disadvantaged populations. The 2002 colloquium, *Global Vaccine Shortage: The Threat to Children and What to Do About It*, identified the four priority issues for which feasible solutions could be found: Stockpiling,



Meier House Provides housing accommodations for meeting participants at Banbury Center.

International Commission on Harmonization (ICH) on Vaccines, Financing, and Public Advocacy. L. Miller (Intermedica, Inc.) and N. Tomich (U.S. Medicine Institute) convened the 2003 colloquium, Feasible Solutions to Global Vaccine Shortages, to propose ways to tackle these issues. The meeting was funded by the Albert B. Sabin Vaccine Institute through a grant from the Bill and Melinda Gates Foundation.

Eugenics

The Ethical, Legal, and Social Issues (ELSI) division of the National Human Genome Research Institute provided funds for *An Image Archive of the American Eugenics Movement* (Dolan DNA Learning Center). Part of the grant was to be used for meetings introducing opinion leaders and policy-makers from government, science, healthcare, education, and the mass media to this episode in American social history. The meeting in 2003 was the last in this series. Organized by D. Micklos (Dolan DNA Learning Center) and myself, the emphasis of the meeting changed a little so as to include contemporary issues. *Eugenics, Genes, and Human Behavior* ranged from a presentation on Sir Francis Galton, through the eugenics movement of 1910–1940, to present-day efforts to find genes affecting human behavior.

Watson School of Biological Sciences

Of the two Topics in Biology Courses for students in the Watson School, the first was a repeat of the course on *Evolution* taught by N. Patel (University of Chicago). The second course was a new one on *Animal Behavior*, taught by H.K. Reeve from Cornell. This, like the others in the program, was tremendously successful, with students observing the behavior of solitary wasps on the Banbury estate, as well as the behavior of larger animals at the Bronx Zoo.

Acknowledgments

The continuing success of the Banbury Center program is due to the efforts of many people: Bea Toliver and Ellie Sidorenko in the Banbury office, Katya Davey at Robertson House, and Chris McEvoy, Joe Ellis, and Danny Maxfield looking after the grounds. All worked very hard to keep the Center running. Food and Beverage Services, Audiovisual, Housekeeping Services, and the Meetings Office had key roles in the smooth operation of the Center. The meetings could not take place without the hard work of the organizers, the generosity of the Laboratory's Corporate Sponsors, and the other donors who funded our meetings, and the Laboratory's scientists who continue to support the Center.

Jan Witkowski

MEETINGS

Toward Understanding the Cellular and Molecular Mechanisms of Medically Unexplained Fatigue

February 23-26

FUNDED BY

Centers for Disease Control & Prevention and The CFIDS Association of America

ARRANGED BY

W.C. Reeves, Centers for Disease Control & Prevention, Atlanta, Georgia
S.D. Vernon, Centers for Disease Control & Prevention, Atlanta, Georgia
C. Heim, Emory University School of Medicine, Atlanta, Georgia

Introduction: S.D. Vernon, Centers for Disease Control & Prevention, Atlanta, Georgia

SESSION 1: Setting the Stage: Chronic Fatigue and the State-of-the-Science Chairpersons: B. Evengard, Karolinska Institutet, Stockholm, Sweden; U. Vollmer-Conna, University of New South Wales, Sydney, Australia

- S. Wessely, Institute of Psychiatry, London, United Kingdom: The spectrum of ailments in medically unexplained fatiguing illnesses and why a multidisciplinary, integrated approach is necessary to further our understanding.
- W.C. Reeves, Centers for Disease Control & Prevention, Atlanta, Georgia: Conservative estimates of the magnitude of medical unexplained fatigue.
- P.D. White, St. Bartholomew's Hospital, London, United
- Kingdom: Cognitive, behavioral, and emotional factors in chronic fatigue.
- D. Papanicolaou, Emory University School of Medicine, Atlanta, Georgia: Neuroendocrine perturbations in chronic fatigue.
- A. Lloyd, University of New South Wales, Sydney, Australia: Acute infection, immunologic perturbations, and chronic fatigue.

SESSION 2: Influences on the Structure and Function of the Brain Chairpersons: E.R. Unger, Centers for Disease Control & Prevention, Atlanta, Georgia; A.H. Miller, Emory University School of Medicine, Atlanta, Georgia

- J.C. de la Torre, University of California, San Diego, Escondido: Cerebral perfusion and neurometabolicsynaptic activity in normal and abnormal states: Relevance to CFS?
- C.D. Sladek, University of Colorado Health Sciences Center, Denver: Regulation of the neurohypophyseal system: Neurotransmitter, neuropeptide, and steroid hormone interactions.



S. Vernon

SESSION 3: Infection, Immunity, Sex, and the Brain Chairperson: M.A. Fletcher, University of Miami School of Medicine, Florida

E. M. Sternberg, National Institute of Mental Health, Bethesda, Maryland: Neuroendocrine regulation of immunity.P.H. Patterson, California Institute of Technology, Pasadena: Maternal infection, fetal brain development, and health.

I. Hickie, St. George Hospital, Sydney, Australia: Persistent infection and immunity and chronic consequences.

SESSION 4: In Search of a Marker: Analytical Approaches Applicable to Medically Unexplained Fatigue

Chairpersons: K. Kenney, The CFIDS Association of America, Charlotte, North Carolina; E. Hanna, National Institutes of Health, Bethesda, Maryland

- A.J. Cleare, Guy's, King's and St. Thomas' School of Medicine, London, United Kingdom: What pyschopharmacology tells us about the pathophysiology of medically unexplained fatigue.
- S. Vernon, Centers for Disease Control & Prevention, Atlanta, Georgia: Biomarker discovery in illness with no lesion.
- S. Shriver, Penn State University, University Park: X versus Y: Sex-based disease differences.
- C. Artlett, Thomas Jefferson University, Philadelphia, Pennsylvania: Microchimerism: Incidental by-product of pregnancy or active participant in human health?

SESSION 5: Can We Explain What Might be Happening in the Brain? **Chairperson: J.F. Jones,** National Jewish Medical & Research Center, Denver, Colorado

Workshop Committee Chairperson: E.R. Unger, Centers for Disease Control & Prevention, Atlanta, Georgia

Summary Report: Future Research Directions



P. White, S. Wessely

Taxonomy and DNA

March 9-12

FUNDED BY

Alfred P. Sloan Foundation

ARRANGED BY

R. DeSalle, American Museum of Natural History, New York

S. Federhen, National Library of Medicine, NIH, Bethesda, Maryland

P. Hebert, University of Guelph, Ontario, Canada

SESSION 1: Species: Biology's Fundamental Particles

Review of Key Questions for Session

N. Knowlton, University of California, San Diego: Marine biodiversity: Marrying DNA and natural history.

B. Golding, McMaster University, Hamilton, Canada: The nature of substitutions that distinguish species.

K.L. Shaw, University of Maryland, College Park: DNA variation in newly evolved species.

J. Hanken, Harvard University, Cambridge, Massachusetts: Cryptic biodiversity: Molecular and morphological approaches.

Discussion of Session

Comments by Discussion Leaders: G. Caccone, Yale University, New Haven, Connecticut; G. Amato, Wildlife Conservation Society, Bronx, New York

SESSION 2: Probing Life's Diversity with DNA

Review of Key Questions for Session

N. Pace, University of Colorado, Boulder: The large-scale structure of the Tree of Life.

M. Sogin, The Marine Biological Society, Woods Hole, Massachusetts: Molecular evolution of eukaryotes: A protist perspective. P. Hebert, University of Guelph, Ontario, Canada: Microgenomics and animal diversity.

Discussion of Session

Comments by Discussion Leaders: K. de Queiroz, Smithsonian Institution, Washington, D.C.; A. Vogler, The Natural History Museum, London, United Kingdom

SESSION 3: Large-scale Biology I

R. McCombie, Cold Spring Harbor Laboratory: Genome projects: A PI's perspective.

SESSION 4: The Analytical Engines

Review of Key Questions for Session

D. Hillis, University of Texas, Austin: The Tree of Life and its role in automated species identification.

K. Crandall, Brigham Young University, Provo, Utah: Bioinformatics methods for large-scale phylogenetics.

R. DeSalle, American Museum of Natural History, New York: Phylogenetic systematics and diagnosis.

Discussion of Session

Comments by Discussion Leaders: A. Bucklin, University of New Hampshire, Durham; B. Schierwater, ITZ, Ecology of Evolution, Hanover, Germany



G. Caccone, K. Shaw, K. Crandall

SESSION 5: Collections of Life

Review of Key Questions for Session

- B. Thiers, New York Botanical Garden, Bronx, New York: Herbaria and systematics: Past, present, and future.
- S. Federhen, National Library of Medicine, NIH, Bethesda, Maryland: Linking sequences to specimens.
- M. O'Leary, Stony Brook University, New York: MorphoBank.
- D. Janzen, University of Pennsylvania, Philadelphia: Reflections on large-scale biodiversity inventories.

Discussion of Session

Comments by Discussion Leaders: W. Hallwachs, University of Pennsylvania, Philadelphia; M. Stoeckle, Cornell University Medical College, Ithaca, New York

SESSION 6: Large-scale Biology II

N. Zinder, The Rockefeller University, New York: Genome projects: Money and politics.

SESSION 7: Group Discussions

Group 1: Acquiring Specimens for DNA Analysis and Acquiring DNA Sequences

Leaders: F. Grassle, Rutgers University, New Brunswick, New Jersey; **K.L. Shaw,** University of Maryland, College Park

Group 2: Analyzing the DNA Sequences and Project Delineation

Leaders: D. Hickey, University of Ottawa, Ontario, Canada; R. DeSalle, American Museum of Natural History, New York

Reports and Discussion
Chairperson: P. Hebert, University of Guelph, Ontario,
Canada



M. Sogin, J. Ausubel

Quantitative Genetic Networks

March 16-19

FUNDED BY

Center for Cancer Research, National Cancer Institute

ARRANGED BY

S. Adhya, National Cancer Institute, NIH, Bethesda, Maryland D.L. Court, National Cancer Institute, Frederick, Maryland

A. Oppenheim, Hebrew University, Hadassah Medical School, Jerusalem, Israel

SESSION 1: λ: CII and CIII

Chairperson: A.M. Campbell, Stanford University, California

A.M. Campbell, Stanford University, California: What do we know—not know about CII?

A. Oppenheim, Hebrew University, Hadassah Medical School, Jerusalem, Israel: CII and CIII in the genetic networks.

P. Parrack, Bose Institute, Kolkata, India: CII stability and transcriptional control: Structural insights and functional implications.

R. Weiss, Princeton University, New Jersey: Rational design and directed evolution strategies for constructing synthetic gene networks.

 S. Adhya, National Cancer Institute, NIH, Bethesda, Maryland: λ's lifestyle decision: Stochastic or deterministic?

SESSION 2: λ: CI and Cro

Chairperson: S. Adhya, National Cancer Institute, NIH, Bethesda, Maryland

G. Gussin, University of Iowa, Iowa City: Quantitative aspects of regulation of the PRM promoter.

J.W. Little, University of Arizona, Tucson: Genetic circuitry: Are its features essential or refinements to a basic ground plan?

I. Dodd, University of Adelaide, Australia: Role of Cro in the

bistable switch.

S.L. Svenningsen, University of Copenhagen, Denmark: Insights into the role of Cro and OL in regulation of PR.

K. Shearwin, University of Adelaide, Australia: The longrange interaction between OL and OR.



SESSION 3: λ: Genetics Circuitry and Modeling

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

- S. Brown, University of Copenhagen, Denmark: Single cell analysis of phophage stability. S. Roy, Bose Institute, Calcutta, India: CI property: A new look at the genetic switch
- K. Sneppen, NORDITA, Copenhagen, Denmark: Modeling

OL-OR derepression and stability.

M.B. Elowitz, The Rockefeller University, New York: Synthetic gene networks and genetic noise in cells.

D.L. Court, National Cancer Institute, Frederick, Maryland: Effect of genes from PL operon on everything else.

SESSION 4: Other Aspects of λ

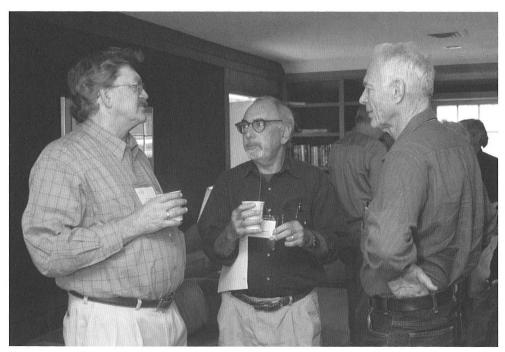
Chairperson: H. Eisen, Seattle, Washington

- M.E. Gottesman, Columbia University, New York: Exclusion of λ by phage HK022.
- L. Thomason, National Cancer Institute, Frederick, Maryland: Role of *rex* and *ren* genes.
- R. Young, Texas A&M University, College Station: Lysis timing: Diverse solutions to the paramount regulatory problem.
- J.R. Roth, University of California, Davis: Effect of prophage on induction of the SOS system and the activity of RecA co-protease.
- J. Stavans, Weizmann Institute of Science, Rehovot, Israel: The SOS response of single cells.

SESSION 5: Other Phages

Chairperson: A. Das, University of Connecticut, Farmington

- L. Orosz, Eotvos Lorand University, Budapest, Hungary: Rhizobium phage 16-3: DNA looping; two immunity regions.
- E. Haggard, Stockholm University, Sweden: Comparison of the genetic switches in P2-related phages.
- K. Hammer, BioCentrum-DTU, Lyngby, Denmark: The genet-
- ic switch in lactococcal phage TP901-1.
- R. d'Ari, Institut Jacques Monod, Paris, France: Does phage Mu gemA gene affect cell cycle?
- D. Endy, Massachusetts Institute of Technology, Cambridge: Phage T7.



J. Roth, M. Gottesman, A. Campbell

Toward a More Unified Understanding of Infectious Disease

March 23-26

FUNDED BY

Burroughs Wellcome Fund

ARRANGED BY

V. McGovern, Burroughs Wellcome Fund, Research Triangle Park, North Carolina

S.L. James, The Ellison Medical Foundation, Bethesda, Maryland

Opening Remarks:

V. McGovern, Burroughs Wellcome Fund, Research Triangle Park, North Carolina

SESSION 1: Overview

E.C. Bond, Burroughs Wellcome Fund, Research Triangle Park, North Carolina

SESSION 2: Current Needs and Expectations: Pathogenesis Research and the Development of Vaccines/Drugs/ Diagnostics

A. Mahmoud, Merck & Co., Inc., Whitehouse Station, New Jersey

SESSION 3: Current Research Perspectives: "Classical" Infectious Diseases

G.I. Miller, Jr., Yale University School of Medicine, New Haven, Connecticut

K. Haldar, Northwestern University Feinberg, Chicago, Illinois

A. Casadevall, Albert Einstein College of Medicine, Bronx, New York

P. Small, University of Tennessee, Knoxville

SESSION 4: Current Research Perspectives: Infectious Roots of Chronic Diseases

M.J. Blaser, New York University School of Medicine, New York

R.H. Yolken, John Hopkins University, Baltimore, Maryland M.V. Pletnikov, Johns Hopkins University School of Medicine, Baltimore, Maryland

SESSION 5: Group Discussion: What Are The Current Expectations for Infectious Disease Research?

Discussion Leader: G.I. Miller, Jr., Yale University School of Medicine, New Haven, Connecticut

SESSION 6: What We Heard—Summary of First Day

Discussion Leader: G.I. Miller, Jr., Yale University School of Medicine, New Haven, Connecticut

SESSION 7: What Could We Gain from a Broader Perspective: Successes and Barriers

N.M. Agabian, University of California, San Francisco

J. Heitman, Duke University, Durham, North Carolina

F. Sher, NIAID, National Institutes of Health, Bethesda, Maryland

M.K. Hostetter, Yale University School of Medicine, New Haven, Connecticut

T.L. Doering, Washington University School of Medicine, St. Louis, Missouri

J.H. McKerrow, University of California, San Francisco



SESSION 8: Group Discussion

- J. Heitman, Duke University Medical Center, Durham, North Carolina
- F. Sher, NIAID, National Institutes of Health, Bethesda, Maryland

SESSION 9: What's in the Toolbox?

- G.M. Weinstock, Baylor College of Medicine, Houston,
- T.B. Kepler, Duke University, Durham, North Carolina P. Kelling, University of British Columbia, Vancouver, B.C., Canada
- M.-W. Tan, Stanford University, California

SESSION 10: Group Discussion

- **Discussion Leader: K. Haldar,** Northwestern University Feinberg School of Medicine, Chicago, Illinois
- R. Rabinovich, Bill & Melinda Gates Foundation, Seattle, Washington: Hopes and aspirations of the Bill & Melinda Gates Foundation.

SESSION 11: What We Heard

- **Discussion Leaders: F. Sher,** NIAID, National Institutes of Health, Bethesda, Maryland and **K. Haldar,** Northwestern University Feinberg School of Medicine, Chicago, Illinois
- **SESSION 12:** Putting the Ideas into Action—What Can Funders Do?
- P. Sager, National Institute of Allergy & Infectious Diseases, Bethesda, Maryland
- W.R. Galey, Howard Hughes Medical Institute, Chevy Chase, Maryland
- V. McGovern, Burroughs Wellcome Fund, Research Triangle Park, North Carolina
- S.L. James, The Ellison Medical Foundation, Bethesda, Maryland

SESSION 13: Group Discussion

- A. Mahmoud, Merck & Co., Inc., Whitehouse Station, New Jersey
- S.L. James, The Ellison Medical Foundation, Bethesda, Maryland



F. Sher, E. Bond, A. Mahmond

Synaptic Function in Fragile-X

March 30-April 2

FUNDED BY

National Institute of Mental Health, NIH, through a grant to FRAXA Research Foundation

ARRANGED BY

M.F. Bear, Howard Hughes Medical Institute, Brown University, Providence, Rhode Island

M.R. Tranfaglia, FRAXA Research Foundation, Newburyport, Massachusetts

Opening Remarks:

M.R. Tranfaglia, FRAXA Research Foundation, Newburyport, Massachusetts and K. Clapp, FRAXA Research Foundation Newburyport, Massachusetts: Patient/clinical perspective

M.F. Bear, Howard Hughes Medical Institute, Brown University, Providence,

Rhode Island: An mGluR hypothesis of mental retardation

SESSION 1: Dendritic RNA Protein Synthesis and Structural Plasticity **Chairperson: W.T. Greenough,** University of Illinois, Urbana

J. Yin, Cold Spring Harbor Laboratory: Synaptic tagging hypothesis applied to Fragile-X.

G.J. Bassell, Albert Einstein College, Bronx, New York: Regulation and mechanism of FMRP trafficking in dendrites. Steward, University of California, Irvine: Targeting mRNA to synaptic sites on dendrites.

J.R. Fallon, Brown University, Providence, Rhode Island: Translational regulation of the Fragile-X message.

SESSION 2: Dendritic RNA Protein Synthesis and Structural Plasticity (Continued)
Chairperson: M.F. Bear, Howard Hughes Medical Institute, Brown University, Providence, Rhode Island

I.J. Weiler, University of Illinois, Urbana-Champaign: Regulation of protein synthesis at the synapse.
K.M. Huber, University of Texas Southwestern Medical Center, Dallas: Effects of mGIR1 and MGluR5 antagonists on long-term depression in hippocampal area CA1.
P.W. Vanderklish, Scripps Research Institute, La Jolla, California: Relationships between synaptic structure and dendritic translation.

W.T. Greenough, University of Illinois, Urbana: Structural consequences of the absence of FMRP.

B. Oostra, Erasmus Universiteit Rotterdam, The Netherlands: Role of FMRP in the dendrite.

E. Khandjian, Hospital St. Francois dAssise, Universite Lavel, Quebec, Canada: Models of Fragile-X syndrome.



D. Stevenson, A. Caudy, M.A. Busby

SESSION 3: mGluRs

Chairperson: K.M. Huber, University of Texas Southwestern Medical Center, Dallas

- R.K.S. Wong, Stony Brook University, New York, Health Science Center, Brooklyn: Group I metabotropic glutamatereceptor-mediated epileptogenesis in the cortex.
- R.P. Bauchwitz, St. Luke's–Roosevelt Institute of Health Sciences, Columbia University, New York: Effects of the mGluR antagonist MPEP in the fmr1-tm1Cgr Fragile-X mouse.

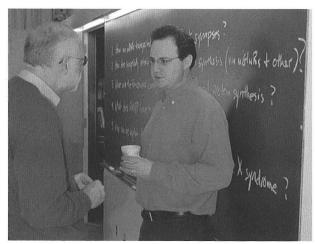
SESSION 4: Ampa Receptor Regulation Chairperson: O. Steward, University of California, Irvine

- R. Malinow, Cold Spring Harbor Laboratory: AMPA receptor trafficking and synaptic plasticity.
- M.F. Bear, Howard Hughes Medical Institute, Brown University, Providence, Rhode Island: AMPA receptor regulation during hippocampal LTD.
- D.J. Linden, Johns Hopkins University School of Medicine, Baltimore, Maryland: Molecular basis of cerebellar longterm synaptic depression.
- P.L. Carlen, Toronto Western Hospital, Canada: Reduced
- SESSION 5: Biology of FMRP Chairperson: I.J. Weiler, University of Illinois, Urbana
- S.T. Warren, Howard Hughes Medical Institute, Emory University School of Medicine, Atlanta, Georgia: Introduction to the biology of FMRP.
- J. Darnell, The Rockefeller University, New York: RNA targets of the FMRP protein.
- A. Beckel-Mitchener, Beckman Institute, Urbana, Illinois: FMRP target mRNAs and their potential functions.
- D. Zarnescu, Emory University, Atlanta, Georgia: Penelope is

- W. Spooren, Hoffman-La Roche, Basel, Switzerland: Behavioral pharmacology of mGlu5 receptor antagonists: Implications for the treatment of anxiety disorders.
- F. Gasparini, Novartis Pharma AG, Basel, Switzerland: Discovery and characterization of ligands for the group I mGluRs: Agonists, antagonists, allosteric positive modulators, allosteric negative modulators, neutral ligands.
- cortical, but no hippocampal LTP, in the FMR1 gene knockout mouse is associated with decreased expression of the cortical GluR1.
- J.R. Larson, University of Illinois, Chicago: Olfactory learning and memory in a mouse model for Fragile-X.
- E. Berry-Kravis, Rush Children's Hospital, Toronto, Canada: AMPA receptor activator (Ampakine) CX516 and Fragile-X syndrome.
- the major autosomal modifier of *Drosophila* Fmr1 overexpression in the eye.
- A. Caudy, Cold Spring Harbor Laboratory: Drosophila Fragile-X-related protein associates with the RNA interference machinery.
- D.L. Nelson, Baylor College of Medicine, Houston, Texas: Developing phenotypic assays in mouse and fly models of deficiencies in FMR1 and related genes.

SESSION 6: Conclusion

M.F. Bear, Howard Hughes Medical Institute, Brown University, Providence, Rhode Island and W.T. Greenough, University of Illinois, Urbana: Wrap-up and discussion



B. Oostra, G. Bassell



D. Nelson, S. Warren

Taking Cancer Genomics to the Clinic

April 13-15

FUNDED BY

Affymetrix, Inc.

ARRANGED BY

T. Kreiner, Affymetrix, Inc., Santa Clara, California

T. Golub, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts

D. Dalma-Weiszhausz, Affymetrix, Inc., Santa Clara, California

SESSION 1: State of Cancer Genomics

T. Kreiner, Affymetrix, Inc., Santa Clara, California: Background of meeting.

P. Meltzer, National Human Genome Research Institute, NIH, Bethesda, Maryland: Translational implications of expression profiling in sarcomas and breast cancer.

T. Golub, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts: Overview of the meeting.

SESSION 2: Current State of Cancer Genomics
Chairperson: T. Golub, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts

P. Meltzer, National Human Genome Research Institute, NIH, Bethesda, Maryland: Introduction.

L.M. Staudt, National Cancer Institute, Bethesda, Maryland: Molecular diagnosis and outcome prediction in lymphoid malignancies by gene expression profiling.

J.R. Downing, St. Jude Children's Research Hospital,

Memphis, Tennessee: Gene expression profiling in acute leukemias: Clinical applications.

S. Ramaswamy, Dana-Farber/Whitehead, Cambridge, Massachusetts: Multiclass molecular diagnosis and staging of cancer patients.



SESSION 3: Technology Platform
Chairperson: W.H. Koch, Roche Molecular Systems,
Alameda, California

- W.H. Koch, Roche Molecular Systems, Alameda, California: Introduction.
- J. Baker, Genomic Health, Inc., Redwood City, California: Determination of tumor gene expression profiles using fixed paraffin-embedded specimens.
- R. Carlson, Vysis Inc., Downers Grove, Illinois: Application of genomic microarrays and FISH to disease management.
- T. Orntoft, Aarthus University Hospital, Denmark:
 Classification of bladder cancer using gene expression.
- M. Rubin, Brigham and Women's Hospital, Boston, Massachusetts: Development of a prostate cancer biomarkers to monitor disease progression.
- J. Warrington, Affymetrix, Inc., Santa Clara, California: Array-based treatment management assays.
- E.F. Petricoin, Food and Drug Administration, Bethesda, Maryland: Serum proteomic pattern diagnostics: Moving to clinical applications.

SESSION 4: FDA Perspectives

E. Mansfield, Food and Drug Administration, Rockville, Maryland: FDA/CDRH Office of in vitro devices: New draft guidance for microarrays and multiplex tests. SESSION 5: Clinical Trials and Validation Challenges
Chairperson: T.J. Triche, Children's Hospital, Los Angeles,
California

- T.J. Triche, Children's Hospital, Los Angeles, California: Introduction.
- A.J. Buckler, Ardais Corporation, Lexington, Massachusetts: Setting standards for clinical genomics in ostic and therapeutic discovery and development.
- J.M. Olson, Fred Hutchinson Cancer Research Center, Seattle, Washington: New therapies based on genomic studies.
- M. van de Vijver, The Netherlands Cancer Institute, Amsterdam: Gene expression profiling to predict outcome in breast cancer.
- E. Feigal, National Cancer Institute, Bethesda, Maryland: NCI initiatives to accelerate movement of genomics to the clinic.

SESSION 6: Review and Summary

Discussion Leaders: T. Kreiner, Affymetrix, Inc., Santa Clara, California; **T. Golub,** Whitehead Institute for Biomedical Research, Cambridge, Massachusetts

Formal Languages for Biological Processes

April 20-23

FUNDED BY Cold S

Cold Spring Harbor Laboratory Corporate Sponsor Program

ARRANGED BY

D. Endy, Massachusetts Institute of Technology, Cambridge **A. Finney,** University of Hertfordshire, Herts, United Kingdom

Y. Lazebnik, Cold Spring Harbor Laboratory

SESSION 1: Do We Need Formal Representations of Biological Systems?

Chairperson: D. Eddy, Massachusetts Institute of Technology, Cambridge

R. Brent, The Molecular Sciences Institute, Berkeley, California: Natural language representations of intracellular biological processes.

M. Wigler, Cold Spring Harbor Laboratory: Say What?F. Cross, The Rockefeller University, New York: Cell cycle control: Complex, or just complicated?

P.A. Silver, Dana Farber Cancer Institute, Boston, Massachusetts: Connecting the genome to the cytoplasm.

General Discussion: Challenges Facing Useful Representations

SESSION 2: Biological Systems and Representations Thereof I **Chairperson: Y. Lazebnik,** Cold Spring Harbor Laboratory

- R. Iyengar, Mount Sinai Medical Center, New York: The activity of biochemical signaling networks and the origins of spatial domains.
- D. Chklovskii, Cold Spring Harbor Laboratory: Search for multineuron modules in *C. elegans* brain.
- S.J. Wodak, Universite Libre de Bruxelles, Brussels, Belgium: Representing and analyzing molecular interactions and cellular processes.
- K.W. Kohn, National Cancer Institute, Bethesda, Maryland: Representation of bioregulatory networks and the origins of spatial domains.
- R. Maimon, Gene Network Sciences, Ithaca, New York: Diagrammatic notation and computation grammar for gene networks.

General Discussion: Limits of Current Representations?

 F. Frankel, Massachusetts Institute of Technology, Cambridge: Envisioning science.



F. Frankel, M. Hucka, Y. Lazebnik, S. Wodak

SESSION 3: Biological Systems and Representations Thereof II Chairperson: R. Brent, The Molecular Sciences Institute, Berkeley, California

- H. Bolouri, Institute for Systems Biology, Seattle, Washington: Appropriate representations for modeling genes and genetic regulatory networks.
- D.L. Cook, University of Washington, Seattle: BioD: Basis for an ontology of biological functions?
- V. Schachter, Genoscope, Evry, France: Formal languages for core molecular biology.
- P.F. Nielsen, University of Auckland, New Zealand: Ontologies for describing biological processes.
- A. Gilman, Lawrence Berkeley National Laboratory, California: The Berkeley BioSPICE conceptual framework: Representing formal and informal knowledge with multiple degrees of detail.
- A. Regev, Harvard University, Cambridge, Massachusetts: Life of Pi: Process algebras as calculi for biomolecular processes.

General Discussion: Limits of Current Representations?

SESSION 4: Integrated Biological Modeling Environments Chairperson: H. Bolouri, Institute for Systems Biology, Seattle, Washington

- T. Sakurada, Keio University, Tsuruoka, Japan: The E-Cell modeling environment.
- J. Schaff, University of Connecticut Health Center, Farmington: The Virtual Cell project.
- B. Mishra, Courant Institute, New York University, New York: Cell talk/Sympatica.
- C. Shaffer, Virginia Tech, Blacksburg: User interface paradigms for describing pathway models.

General Discussion: Future Requirements and Path Forward

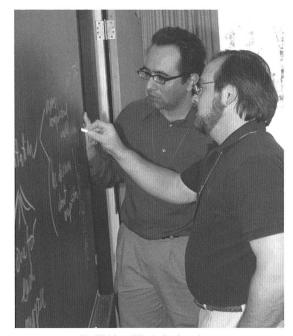
SESSION 5: Languages Underlying Representation and Community Issues **Chairperson: A. Finney,** University of Hertfordshire, Herts, United Kingdom

- A. Finney, University of Hertfordshire, Herts, United Kingdom: Systems biology markup language: Level 2 and beyond.
- J. Ambrosiano, Los Alamos National Laboratory, New Mexico: Rule-based models: Compact representation of large cellular networks.
- J. Webb, BBN Technologies, Cambridge, Massachusetts: Language design considerations for composite models of biological systems.
- J. Cassatt, National Institute of General Medical Sciences, Bethesda, Maryland: Mathematics, engineering, physics, and biology: Challenges for funding agencies.

General Discussion: Flourishing Orthography?

Closing Remarks:

- **D. Endy,** Massachusetts Institute of Technology, Cambridge
- **A. Finney,** University of Hertfordshire, Herts, United Kingdom
- Y. Lazebnik, Cold Spring Harbor Laboratory



D. Chklovskii, J. Ambrosiano

Neural Circuits: Principles of Design and Operation

April 27-30

FUNDED BY

The Swartz Foundation

ARRANGED BY

K.D. Miller, University of California, San Francisco

H.S. Seung, Massachusetts Institute of Technology, Cambridge

SESSION 1: General Circuit Properties

Chairperson: D. Kleinfeld, University of California, San Diego

- D. Chklovskii, Cold Spring Harbor Laboratory: (Potential) connectivity in cortical circuits.
- S. Laughlin, University of Cambridge, United Kingdom: Stochastic limits to the design of energy-efficient neural circuits.

SESSION 2: General Cortical Properties I
Chairperson: J.A. Hirsch, University Southern California,
Los Angeles

- R. Yuste, Columbia University, New York: Imaging the structure and dynamics of the cortical microcircuit.
- L.F. Abbott, Brandeis University, Waltham, Massachusetts: Controlling and supervising cortical circuits.
- J.C. Hawkins, Redwood Neuroscience Institute, Menlo Park, California: General mechanisms of neocortical memory.
- S. Makeig, University of California, San Diego: Are brain circuits multiscale?

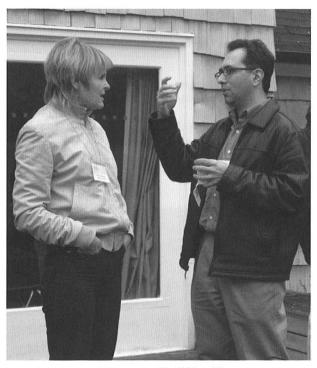
SESSION 3: General Cortical Properties II
Chairperson: J.A. Hirsch, University of Southern California,
Los Angeles

- H. Markram, Brain & Mind Institute, Lausanne, Switzerland: Molecular basis of electrical diversity of interneurons.
- G. Tamas, University of Szeged, Hungary: Sources and targets of slow inhibition in the neocortex.
- A.M. Thomson, University of London School of Pharmacy, London, United Kingdom: Frequency and pattern filtering at cortical synapses.

SESSION 4: Visual Cortex I

Chairperson: L.F. Abbott, Brandeis University, Waltham, Massachusetts

- A. Bell, Redwood Neuroscience Institute, Menlo Park, California: Nonlinear, multilayer ICA and the cortical visual processing hierarchy.
- E.M. Callaway, The Salk Institute for Biological Studies, La Jolla, California: Functional organization of color-opponent input to primary visual cortex.
- D.L. Ferster, Northwestern University, Evanston, Illinois: Testing models of visual cortical function.



A. Thomson, D. Chklovskii

SESSION 5: Visual Cortex II

Chairperson: L.F. Abbott, Brandeis University, Waltham, Massachusetts

- Y. Fregnac, Institut Alfred Fessard-CNRS, Gif sur Yvette, France: Shunting inhibition and computational diversity in visual cortex.
- J.A. Hirsch, University of Southern California, Los Angeles: Inhibitory circuits at the first stage of visual cortical processing.
- J.S. Lund, University of Utah, Salt Lake City: Real-life visual cortical circuits as substrates for its functional properties.
- K.D. Miller, University of California, San Francisco: Role of dominant feedforward inhibition in cat V1 layer 4.
- M. Shelley, New York University, New York: Coarse-graining of neuronal networks and the visual cortex.

SESSION 6: Nonvisual Cortical/Forebrain Systems

Chairperson: H. Markram, Brain & Mind Institute, Lausanne, Switzerland

- D. Kleinfeld, University of California, San Diego: Attention, filtering, and mixing: Nonlinear coding blocks in the rat somatosensory motor system.
- C. Brody, Cold Spring Harbor Laboratory: A computational model of the mammalian olfactory bulb.
- J.J. Hopfield, Princeton University, New Jersey: Deriving "learning rules" for spike-timing based computation from the necessity of network self-repair.
- M. Fee, Bell Laboratories, Murray Hill, New Jersey: Neural mechanisms of sequence generation in a songbird.
- H.S. Seung, Massachusetts Institute of Technology,

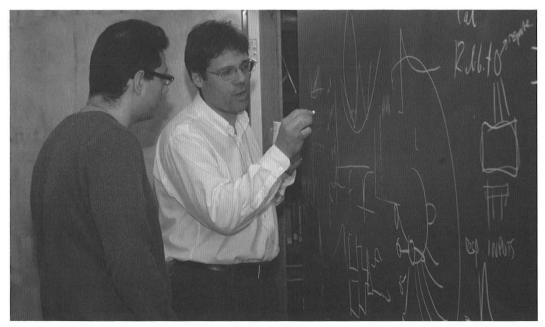
Cambridge: Learning by reinforcement of stochastic synaptic transmission in spiking neural network.

- H.A. Swadlow, University of Connecticut, Storrs: A thalamocortical feedforward inhibitory network: Principles and operations in the awake state.
- X.-J. Wang, Brandeis University, Waltham, Massachusetts: A basic cortical microcircuit model of working memory with three subclasses of inhibitory neurons.
- A. Zador, Cold Spring Harbor Laboratory: Computation in auditory cortex.

SESSION 7: Silicon/Robotics

Chairperson: J.J. Hopfield, Princeton University, New Jersey

- K.A. Boehen, University of Pennsylvania, Philadelphia: From local microcircuits to cortical maps.
- K.K. Likharev, Stony Brook University, New York: CrossNets: Possible molecular electronics neural circuits.
- S.-C. Liu, University and ETH Zurich, Switzerland: Spike-based vision system.
- R. Sarpeshkar, Massachusetts Institute of Technology, Cambridge: Biologically inspired electronics.



C. Brody, M. Fee

Scientific Opportunities in Macromolecular Crystallography at NSLS-II

July 9-10

FUNDED BY

Brookhaven National Laboratory

ARRANGED BY

W. Hendrickson, Howard Hughes Medical Institute, Columbia University, New York

L. Joshua-Tor, Cold Spring Harbor Laboratory

Opening Remarks:

W. Hendrickson, Howard Hughes Medical Institute, Columbia University, New York

L. Joshua-Tor, Cold Spring Harbor Laboratory

SESSION 1

S. Dierker, Light Sources Directorate, Brookhaven National Laboratory, Upton, New York: New storage ring design and characteristics

L. Berman, National Synchrotron Light Source, Brookhaven National Laboratory, Upton, New York: Beamline optics and new detector developments.

SESSION 2

R. MacKinnon, Howard Hughes Medical Institute, The Rockefeller University, New York: Membrane proteins: State of the art, unique problems, and future needs.

SESSION 3

A. Joachimiak, Argonne National Laboratory, Illinois: Structural genomics.

Informal discussion: What Can the Structural Biologists Do to Further Support the Proposal?

SESSION 4

- T. Steitz, Howard Hughes Medical Institute, Yale University, New Haven, Connecticut: Large complexes: Unique issues and future needs.
- J.M. Hogle, Harvard University, Cambridge, Massachusetts: Virus structures.
- P. Fitzgerald, Merck Research Laboratories, Rahway, New Jersey: Structure-assisted drug development.

SESSION 5: Summary and Next Steps

W. Hendrickson, Howard Hughes Medical Institute, Columbia University, New York

L. Joshua-Tor, Cold Spring Harbor Laboratory



W. Weiss, L. Joshua-Tor



W. Hendrickson, T. Steitz, H. Robinson

Taxonomy, DNA, and the Bar Code of Life

September 10-12

FUNDED BY

Alfred P. Sloan Foundation

ARRANGED BY

J. Baker, Academy of Natural Sciences, Philadelphia

J. Hanken, Harvard University, Cambridge, Massachusetts

Welcome and Introduction: J. Baker, Academy of Natural Sciences, Philadelphia, Pennsylvania

J. Hanken, Harvard University, Cambridge, Massachusetts

SESSION 1: DNA-based Species Identification: Conceptual Foundations

Chairperson: J. Hanken, Harvard University, Cambridge, Massachusetts

J.C. Venter, The Center for the Advancement of Genomics, Rockville, Maryland: Environmental shotgun sequencing.R. DeSalle, American Museum of Natural History, New York Recap of Banbury I.

Discussants

M. Stoeckle, The Rockefeller University, New York J. Hanken, Harvard University, Cambridge, Massachusetts

P. Hebert, University of Guelph, Ontario, Canada DNA-based species identification: State of the art.

Discussants

- C. Moritz, University of California, Berkeley
- G. Caccone, Yale University, New Haven, Connecticut
- A. Bucklin, University of New Hampshire
- S. Miller, Smithsonian Institution, Washington, D.C. Are museum collections the appropriate place to begin a large-scale effort?

Discussants

- R. Lane, The Natural History Museum, London, United Kingdom
- G. Rosenberg, Academy of Natural Sciences, Philadelphia, Pennsylvania

SESSION 2: Implementing a DNA Bar-coding Initiative: Strategies, Specimens, Databases, Funding

Chairperson: J. Baker, Academy of Natural Sciences, Philadelphia, Pennsylvania

M. Stoeckle, The Rockefeller University, New York: Organizational strategies: Early action plan vs. museum consortium.

Discussants

- P. Hastings, Scripps Institution of Oceanography, La Jolla, California
- M. Graham, Canadian Museum of Nature, Ottawa, Ontario, Canada
- G. Caccone, Yale University, New Haven, Connecticut
- J.L. Edwards, Global Biodiversity Information Facility, Copenhagen, Denmark



R. Phelan, G. Caccone

Museum specimens: How many are there, and how are they preserved? Which types are most appropriate for a DNA bar-coding effort? Which ones should be avoided?

Discussants

C. Moritz, University of California, BerkeleyS.V. Edwards, University of Washington, SeattleR. DeSalle, American Museum of Natural History, New York Databases.

Discussants

J.L. Edwards, Global Biodiversity Information Facility, Copenhagen, Denmark

S. Federhen, National Library of Medicine, NIH, Bethesda, Maryland

P. Hebert, University of Guelph, Ontario, Canada

J. Baker, Academy of Natural Sciences, Philadelphia, Pennsylvania Costs and funding. How much, and who will pay?

Discussants

J. Omura, The Presidio of San Francisco, California

R. Phelan, All Species Foundation, San Francisco, California

SESSION 3: Establishing Consensus Plans

Chairpersons: J. Baker, Academy of Natural Sciences, Philadelphia, Pennsylvania; J. Hanken, Harvard University, Cambridge, Massachusetts

- Is there life after Banbury II and, if so, what is it? What next?
- Working groups, initial funding strategies, statement of purpose.
- Statement of purpose.



J. Marchioni, D. Janzen, S. Miller, J. Edwards

Integrating Progress in the Genetics and Neuropharmacology of Schizophrenia

September 14-17

FUNDED BY

Cold Spring Harbor Laboratory Corporate Sponsor Program

ARRANGED BY

C.R. Cloninger, Washington University Medical School, St. Louis, Missouri

J.T. Coyle, Harvard Medical School, Belmont, Massachusetts

SESSION 1: Overview of Current Status of the Molecular Genetics of Schizophrenia Chairperson: C.R. Cloninger, Washington University Medical School, St. Louis, Missouri

- C.R. Cloninger, Washington University Medical School, St. Louis, Missouri: General update and overview of the genetics of schizophrenia.
- K. Stefansson, DeCode Genetics, Reykjavik, Iceland: Studies of neuregulin 1 by DeCode.
- A. Corvin, St. James Hospital, Dublin, Ireland and D. Morris, St. James Hospital, Dublin, Ireland: Refinement of the "at
- risk" haplotype for schizophrenia.
- I. Chumakov, Genset, Evry, France: Studies of G72 and DAAO in schizophrenia by Genset.
- D.R. Weinberger, National Institute of Mental Health, NIH, Bethesda, Maryland: Critique of genetics of NMDA hypofunction in schizophrenia.

SESSION 2: Neural Systems Approaches to the NMDA Hypofunction Model of Schizophrenia **Chairperson: J.T. Coyle,** Harvard Medical School, Belmont, Massachusetts

- J.T. Coyle, Harvard Medical School, Belmont, Massachusetts: Overview of NMDA hypofunction model. S. Grant, University of Edinburgh, United Kingdom: A core
- molecular mechanism for cognition and its disorders.

 D. Javitt, Nathan Kline Institute for Psychiatric Research,
- Orangeburg, New York: Interactions of NMDA and dopamine systems and therapeutic targets.
- J.H. Krystal, Yale University School of Medicine, West Haven,
- Connecticut: Interactions of NMDA and serotonin systems and therapeutic targets.
- J.W. Newcomer and N.B. Farber, Washington University School of Medicine, St. Louis, Missouri: Developmental implications of NMDA receptor hypofunction.
- C.A. Tamminga, University of Texas Southwestern Medical Center, Dallas: Critique of status of neuropharmacology of schizophrenia.



J. Coyle, D. Weinberger



J. Watson, R. Cloninger

SESSION 3: Other Genetic and Epigenetic Influences on Risk of Schizophrenia
Chairperson: M.T. Tsuang, Harvard Institute of Psychiatric Epidemiology & Genetics, Journal of
Neuropsychiatric Genetics, Boston, Massachusetts

- M. Owen, University of Wales College of Medicine, Cardiff, United Kingdom: Overview of nonglutamate genetic factors and their interactions influencing the risk of schizophrenia.
- D. Blackwood, The Royal Edinburgh Hospital, United Kingdom: A chromosome 1q locus for schizophrenia.
- S. Leonard, University of Colorado Health Sciences Center,

Denver: $\alpha 7$ nicotinic receptor locus and NMDA interactions in schizophrenia.

R.E. Straub, National Institute of Mental Health, NIH, Bethesda, Maryland: Dysbindin (DTNBP1, 6p22.3): SNP detection, cognitive and fMRI phenotypes, and analysis of transcript and protein levels.

SESSION 4: Technological Opportunities for Accelerating Progress Chairperson: J.W. Olney, Washington University Medical School, St. Louis, Missouri

- M. Laruelle, New York State Psychiatric Institute, Columbia University, New York: Imaging NMDA-DA interactions in working memory and schizophrenia.
- R. Schwarcz, Maryland Psychiatric Research Center, Baltimore: Studying NMDA- α 7 nicotinic interactions with novel mGluR ligands.
- S. Heckers, McLean Hospital, Belmont, Massachusetts:
- Regulation of hippocampal neurons in schizophrenia.
- J. Eberwine, University of Pennsylvania Medical School, Philadelphia: Single cell chip technologies for genomics and proteomics.
- M.A. Geyer, University of California, San Diego: Gluamatergic influences on sensorimotor gating in rodents.

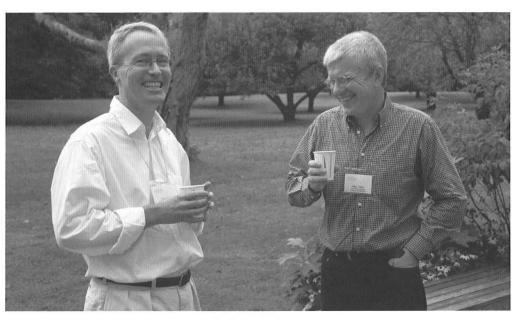
SESSION 5: Where Do We Go from Here to Understand the Clinical Reality of Schizophrenia and Schizotypy?

Chairperson: E.M. Scolnick, Merck Research Laboratories, West Point, Pennsylvania

- M.T. Tsuang, Harvard Institute of Psychiatric Epidemiology
 & Genetics, Journal of Neuropsychiatric Genetics,
 Boston, Massachusetts: A psychiatric geneticist's perspective.
- W.T. Carpenter, University of Maryland, Baltimore: A psychopharmacologist's perspective.
- Pablo Gejman, University of Chicago, Illinois: A molecular geneticist's perspective.

Panel Discussion:

- K. Stefansson, DeCode Genetics, Reykjavik, Iceland
- **D.R. Weinberger,** National Institute of Mental Health, NIH, Bethesda, Maryland
- **J.W. Olney,** Washington University Medical School, St. Louis, Missouri
- **D. Goldman,** National Institute on Alcohol Abuse and Alcoholism, NIH, Rockville, Maryland



S. Grant, M. Owen

Regulation of Inflorescence Morphology: Insights from Genetics and Genomics

September 21-24

FUNDED BY

Cold Spring Harbor Laboratory Corporate Sponsor Program

ARRANGED BY

E.A. Kellogg, University of Missouri, St. Louis **D. Jackson,** Cold Spring Harbor Laboratory

SESSION 1: Getting Started: Control of the Floral Transition Chairperson: T. Rocheford, University of Illinois, Urbana

- G. Coupland, Max-Planck-Institute for Plant Breeding Research, Koeln, Germany: Variation in the mechanisms that control flowering time.
- T. Brutnell, Boyce Thompson Institute, Ithaca, New York: Role of phytochromes in the regulation of flowering time in maize.
- D. Laurie, John Innes Centre, Norwich, United Kingdom: Genetic control of flowering time in barley and wheat.
- M. Edgerton, Monsanto-Ceregen, St. Louis, Missouri: Alteration of flowering time in corn.
- J. Colasanti, University of Guelph, Ontario, Canada: Leafderived floral inductive signals in maize.

SESSION 2: Development Mechanisms I: Inflorescence Structure and Function Chairperson: S. Hake, U.S.D.A. Plant Gene Expression Center, Albany, California

- E.A. Kellogg, University of Missouri, St. Louis: Grass flowers and inflorescences: New interpretations from comparative data.
- K. Ikeda, University of Tokyo, Japan: Inflorescence and spikelet development in rice and functions of the APO gene.
- D. Jackson, Cold Spring Harbor Laboratory: Fasciation and control of seed row number in maize.
- W. Bruce, Pioneer Hi-Bred International, Inc., Johnston, Iowa: Characterizations of a maize *CLAVATA3* functional homolog.



SESSION 3: QTL and Association Mapping Chairperson: R. Martienssen, Cold Spring Harbor Laboratory

- E.S. Buckler, North Carolina State University, Raleigh: Using diverse maize germplasm to dissect inflorescence traits.
- T. Rocheford, University of Illinois, Urbana: QTL approaches
- to study of maize inflorescence architecture.
- D. Zamir, Hebrew University of Jerusalem, Rehovot, Israel: Real-time QTL of yield.

SESSION 4: Molecular Evolution

Chairperson: E. Vollbrecht, Cold Spring Harbor Laboratory

- E. Kramer, Harvard University, Cambridge, Massachusetts: Two roads diverged in a wood: The elusive nature of genetic orthology.
- M.D. Purugganan, North Carolina State University, Raleigh: Molecular evolution of *Arabidopsis* shoot architecture.
- R.M. Clark, University of Wisconsin, Madison: The complexity of selection at a major effect QTL in maize, *teosinte* branched 1 (tb1).
- M. Frohlich, The Natural History Museum, London, United Kingdom: Suggestions for Evo-devo research.

SESSION 5: Developmental Evolution Chairperson: E.A. Kellogg, University of Missouri, St. Louis

- P. Soltis, University of Florida, Gainesville: Sequence analysis and expression patterns of floral genes in basal angiosperms.
- E. Vollbrecht, Cold Spring Harbor Laboratory: *Ramosa1* and branching in the grass inflorescence.
- D. Baum, University of Wisconsin, Madison: Role of meristem identity genes in the parallel evolution of inflorescence architecture in Brassicaceae.
- W. Rottmann, ArborGen, Summerville, South Carolina: Response of sweetgum to overexpression of *LEAFY*.

SESSION 6: Genomics Approaches Chairperson: V. Brendel, Iowa State University, Ames

- R. Lucito, Cold Spring Harbor Laboratory: ROMA: Oligonucleotide arrays for the detection of gene copy number fluctuations.
- V. Brendel, Iowa State University, Ames: Computational approaches to identify candidate genes involved in inflorescence development.
- G. Chuck, USDA, ARS, Albany, California: Microarray analysis of the spikelet meristem identity mutants branched *silkless 1* and *frizzy panicle1* of maize and rice.
- E.D. Brenner, New York University, New York: A genomic approach to study seed development in the basal gymnosperms: Cycads and ginkgo.

SESSION 7: Developmental Mechanisms II: Floral Organ Polarity, Number, and Size Chairperson: D. Jackson, Cold Spring Harbor Laboratory

- E.E. Irish, University of Iowa, Iowa City: Polarity of the maize flower and its imposition by the inflorescence.
- H. Hirano, The University of Tokyo, Japan: Regulation of floral organ number and identity in rice.
- J. Fletcher, USDA Plant Gene Expression Center, Albany, California: Role of *ULTRAPETALA* in regulating *Arabidopsis* shoot and floral meristem activity.
- Y. Eshed, Weizmann Institute of Science, Rehovot, Israel: Regulation of plant organ size: A story of bread and butter.
- S. Hake, USDA Plant Gene Expression Center, Albany, California: Role of meristem size on developmental fate.



M. Timmermans, H. Hirano

The Biology of Neuroendocrine Tumors

September 28-30

FUNDED BY

Verto Institute, LLC

ARRANGED BY

A.J. Levine, Institute for Advanced Studies, Princeton, New Jersey

E. Vosburgh, Verto Institute, LLC, Stamford, Connecticut

Introductory Remarks: A.J. Levine, Institute for Advanced Studies, Princeton, New Jersey: Verto Research Program Overview

SESSION 1: Neural Crest and Neuroendocrine Development Chairperson: T. Jacks, Massachusetts Institute of Technology, Cambridge

J.A. Epstein, University of Pennsylvania, Philadelphia: Using mouse models to elucidate the developmental biology of the neural crest.

S.K. Kim, Stanford University School of Medicine, California: Signaling pathways regulating neuroendocrine cell differentiation and proliferation in the developing pancreas.

M.L. Meyerson, Harvard Medical School, Boston,

Massachusetts: Functional studies of the multiple endocrine neoplasia type I (MEN-1) gene.

Keynote Speaker:

A.J. Levine, Institute for Advanced Studies, Princeton, New Jersey: Autophagy and cancer.

SESSION 2: Neuroendocrine Receptors

Chairperson: L.B. Chen, Dana-Farber Cancer Institute, Lexington, Massachusetts

- G. Rindi, Universita degli Studi, Parma, Italy: VGF expression in the neuroendocrine system and related growths.
- R. Salgia, University of Chicago, Illinois: Role of receptor kinases in neuroendocrine tumors.
- R.V. Lloyd, Mayo Clinic, Rochester, Minnesota: EGFR in neuroendocrine (carcinoid) tumors.
- V. Giandomenico, Uppsala University, Sweden: Identification of carcinoid-associated antigens for vaccine development.
- D. Agrawal, H. Lee Moffitt Cancer Center and University of South Florida, Tampa: Development and utilization of carcinoid cell models for molecular analysis.



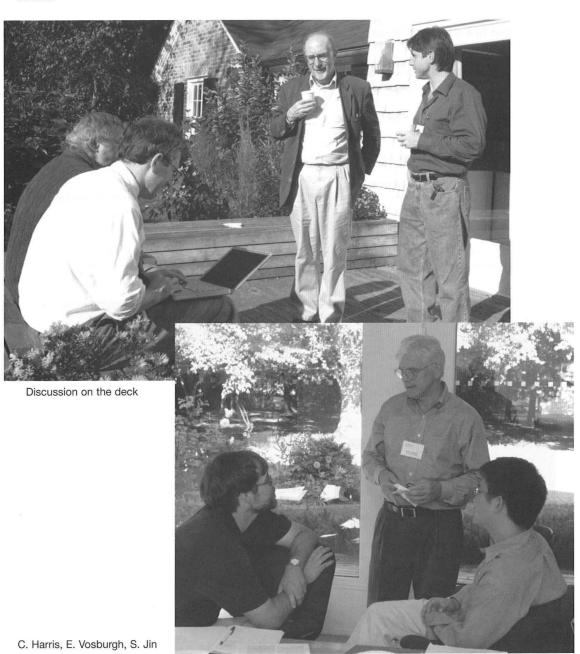
M. Meyerson, A. Levine, K. Peters

SESSION 3: Genetic Association Studies
Chairperson: J. Hoh, Yale University School of Medicine,
New Haven, Connecticut

- J. Ott, The Rockefeller University, New York: Statistical principles of human gene mapping.
- C. Sing, University of Michigan Medical Center, Ann Arbor: Insights from genome association studies of common diseases.

SESSION 4: Clinical Update on Neuroendocrine Cancers **Chairperson: K. Oberg,** University Hospital, Uppsala, Sweden

- K. Oberg, University Hospital, Uppsala, Sweden: Position emission tomograph (PET) in the management of neuroendocrine tumors.
- L. Kvols, H. Lee Moffitt Cancer Center and University of South Florida, Tampa: An update on radiolabled peptide therapy of carcinoid tumors.
- J. Yao, Gastrointestinal Medical Oncology, Houston, Texas: Phase II study of Imatinib in patients with metastatic or unresectable carcinoid tumor.
- M.H. Kulke, Dana-Farber Cancer Institute, Boston, Massachusetts: Clinical trials in neuroendocrine tumors: Role of molecularly targeted therapies.



Mouse Genome-wide Targeted Mutagenesis

September 30-October 1

FUNDED BY

Cold Spring Harbor Laboratory

ARRANGED BY

R.P. Woychik, The Jackson Laboratory, Bar Harbor, Maine C.P. Austin, National Human Genome Research Institute, NIH

Welcome and Summary of Expectations: R.P. Woychik, The Jackson Laboratory, Bar Harbor, Maine

SESSION 1: Define What Type of Mutations Would be Most Desirable in a Genome-wide Collection

Review nature of mutations created by each gene-based mutagenesis technology: Debate pros, cons, and costs of each approach.

Moderator: G.M. Duyk, Exelixis Inc., South San Francisco, California

- Homologous recombination: M.R. Capecchi, University of Utah, Salt Lake City
- Gene-trapping approaches: B. Skarnes, Wellcome Trust Sanger Institute, Cambridge, United Kingdom, and B. Zambrowicz. Lexicon Genetics. The Woodlands. Texas
- RNAi: I.M. Verma, The Salk Institute for Biological Studies, La Jolla, California
- Transgenic approaches/universal integration sites:
 N. Heintz, The Rockefeller University, New York

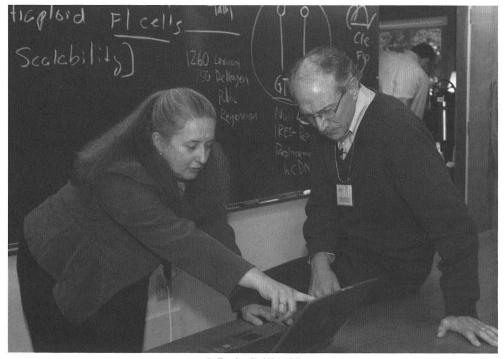
SESSION 2: Desired Scope of the Project

Is there a compelling scientific case to undertake creating mutations in all genes in the genome?

To what extent do the currently available resources begin to address the needs of the biomedical research community? Are current technologies and approaches efficient enough to meet the need, and what would be the time frame for completion?

Moderator: A. Bradley, The Wellcome Trust Sanger Institute, Cambridge, United Kingdom

- High-throughput KO technology: M.W. Moore, Deltagen, Inc., Redwood City, California
- Omnibank approach: A.T. Sands, Lexicon Genetics, The Woodlands, Texas
- Regeneron approach: G.D. Yancopoulos, Regeneron Pharmaceuticals, Inc. Tarrytown, New York
- Summary/Discussion



J. Eppig, R. Woychik

SESSION 3: Define Approaches to Cost Effectively and Efficiently Maintain a Targeted Mutant Mouse Resource

Which reagents (e.g., DNA targeting constructs, ES cells, and frozen embryos) would be available for distribution? What is the cost of maintaining the resource? To what extent should the mutant lines be phenotyped as part of a large-scale effort?

Moderator: T. Magnuson, University of North Carolina, Chapel Hill

- ES cells/chimeras/mice: A. Nagy, University of Toronto, Canada
- Cryopreservation (sperm/ICSI/Frozen embryos): K.C.K. Lloyd, University of California, Davis
- High-throughput phenotyping: M.W. Moore, Deltagen, Inc., Redwood City, California
- Summary/discussion

SESSION 4: Define the Nature of a Project Database, Enduser Needs, Integrating Data into Current Resources, and Intellectual Property Issues

Moderator: J.T. Eppig, The Jackson Laboratory, Bar Harbor, Maine

- Database needs and integration resources: J.T. Eppig, The Jackson Laboratory, Bar Harbor, Maine
- IP and distribution issues: G.M. Duyk, Exelixis, Inc., San Fransicso, California
- Summary/discussion

SESSION 5: Open Discussion/Debate to Define the Scientific Nature of a Large-scale Consensus Project

Moderator: F.S. Collins, National Human Genome Research Institute, NIH, Bethesda, Maryland

We will start with a presentation of a "model project" based on discussions from the preceding sessions. Participants will be asked to modify the model during the course of the discussion to arrive at a final product with which to go forward.

- Nature of the mutations to be generated
- · Scope of the project
- Nature of the resources to be distributed
- Informatics needs
- · IP
- Cost and time line

SESSION 6: Wrap Up, Next Steps
Moderator: R.P. Woychik, The Jackson Laboratory, Bar
Harbor, Maine



A. Roses, M. Moore

Feasible Solutions to Global Vaccine Shortages

October 8-10

FUNDED BY

Albert B. Sabin Vaccine Institute

ARRANGED BY

L.A. Miller, Intermedica, Inc., Darien, Connecticut N.E. Tomich, U.S. Medicine Institute, Washington, D.C.

Welcome: H.R. Shepherd, Albert B. Sabin Vaccine Institute, New Canaan, Connecticut

SESSION 1:

Introductory Remarks: David Heymann, World Health Organization, Geneva, Switzerland: Polio surveillance and immunization program.

Charge to Conference, Conference Co-Chairs:

L.A. Miller, Intermedica, Inc., Darien, Connecticut and **N.E. Tomich,** U.S. Medicine Institute, Washington, D.C.

Keynote Speaker: S. Cochi, National Immunization Program, CDC, Atlanta, Georgia

SESSION 2: Stockpiling

Chairpersons: E. O'Mara, Centers for Disease Control & Prevention, Atlanta, Georgia; S. Bice, Centers for Disease Control & Prevention, Atlanta, Georgia

Task Force Report

Task Force Panel:

S. Cochi, National Immunization Program, Centers for Disease Control & Prevention, Atlanta, Georgia

C.A. deQuadros, Albert B. Sabin Vaccine Institute, Washington, D.C.

D.C. Peterson, Immunization Action Coalition, St. Paul, Minnesota

E. Wilder, National Immunization Program, Centers for Disease Control & Prevention, Atlanta, Georgia

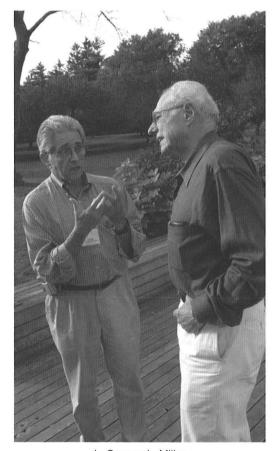
SESSION 3: Open Discussion and Consensus: Stockpiling **Moderators: L.A. Miller,** Intermedica, Inc., Darien, Connecticut; **N.E. Tomich,** U.S. Medicine Institute, Washington, D.C.

SESSION 4: International Commission on Harmonization Chairperson: J. Milstein, University of Maryland School of Medicine, Montpelier, France

Task Force Report

Task Force Panel:

A. Homma, Bio-Manguiinhos/Fiocruz, Rio de Janeiro, Brazil S. Jadhav, Serum Institute of India, Pune S.H. Lee, Center for Biologics Evaluation, Seoul, Korea J.I. Santos, National Immunization Council, Juarez, Mexico



L. Cooper, L. Miller

SESSION 5: Open Discussion and Consensus: ICH Moderators: L.A. Miller, Intermedica, Inc., Darien, Connecticut; N.E. Tomich, U.S. Medicine Institute, Washington, D.C.

SESSION 6: Public Advocacy

Chairperson: J.E. Fischer, Council on Foreign Relations, Washington, D.C.

Task Force Report

Task Force Panel:

- L. Cooper, Columbia University College of Physicians & Surgeons, New York
- S. Feldman, Aventis USA, Swiftwater, Pennsylvania C.M. Grant, Aventis USA, Swiftwater, Pennsylvania
- H. Larson, UNICEF, New York
- R. MacDougall, Albert B. Sabin Vaccine Institute, Inc., Washington, D.C.
- C. Ruppel, Every Child By Two, Washington, D.C.

SESSION 7: Open Discussion and Consensus: Public Advocacy

Moderators: L.A. Miller, Intermedica, Inc., Darien, Connecticut; N.E. Tomich, U.S. Medicine Institute, Washington, D.C. R. Giffin, The National Academies, Washington, D.C.: Key elements of Institute of Medicine Report

SESSION 8: Financing

Chairperson: S. Jarrett, UNICEF, New York

Task Force Report

Task Force Panel:

- D. Braga, Aventis USA, Swiftwater, Pennsylvania
- A. Robbins, Tufts University School of Medicine, Boston, Massachusetts
- J.C. Sadoff, Aeras Global TB Vaccine Foundation, Rockville, Maryland
- D. Salisbury, Skipton House, London, United Kingdom
- L. Tan, American Medical Association, Chicago, Illinois

SESSION 9: Open Discussion and Consensus: Financing

Where Do We Go From Here?
L.A. Miller, Intermedica, Inc., Darien, Connecticut
N.E. Tomich, U.S. Medical Institute, Washington, D.C.
Linking together the consensus statements
Prioritizing the action steps



Eugenics, Genes, and Human Behavior

October 14-16

FUNDED BY

National Human Genome Research Institute, NIH

ARRANGED BY

D. Micklos, Dolan DNA Learning Center, Cold Spring Harbor LaboratoryJ.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory

Introduction:

J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory

D. Micklos, Dolan DNA Learning Center, Cold Spring Harbor Laboratory

SESSION 1: History

Chairperson: S. Selden, University of Maryland, College Park

N. Gillham, Duke University, Durham, North Carolina: Sir Francis Galton and the foundations of eugenics.

E. Carlson, Stony Brook University, New York: Bad seed, corrupted germ plasm, prized pedigrees, and eugenic worth.

SESSION 2: Impacts

Chairperson: D. Micklos, Dolan DNA Learning Center, Cold Spring Harbor Laboratory

P.A. Lombardo, University of Virginia, Charlottesville: Immigration and sterilization in the United States.

G.E. Allen, Washington University, St. Louis: The international influence of the U.S. eugenics movement.

SESSION 3: Behavioral Genetics I

Chairperson: J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory

 C. Gilliam, Columbia University, New York: Searching for genes involved in behavioral disorders.

General Discussion

Moderator: S. Selden, University of Maryland, College Park

SESSION 4: Resources: Dolan DNA Learning Center

D. Micklos and J.A. Witkowski, Cold Spring Harbor Laboratory: Introduction to the Image Archive on the American Eugenics Movement.

SESSION 5: Behavioral Genetics II

Chairperson: J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory

N. Segal, California State University, Fullerton: Twin studies and heritability of behavioral traits.

K.R. Jamison, Johns Hopkins School of Medicine, Baltimore: Personal experiences with mental illness and eugenics.

General Discussion

Moderator: S. Selden, University of Maryland, College Park



N. Gillham, S. Selden



Participants in a discussion

Controlling the Differentiation of Pluripotent Cells

October 19-22

FUNDED BY

Cold Spring Harbor Laboratory Corporate Sponsor Program

ARRANGED BY

R. McKay, National Institute of Neurological Disorders and Stroke, NIH

SESSION 1: Controlling ES Cell Differentiation

Chairperson: N. Benvenisty, The Hebrew University of Jerusalem, Israel

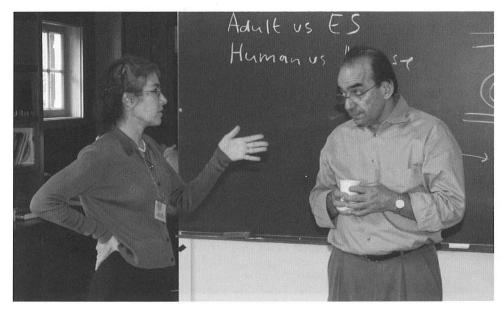
- N. Benvenisty, The Hebrew University of Jerusalem, Israel: Differentiation and genetic manipulation of human embryonic stem cells.
- A. Smith, University of Edinburgh, United Kingdom: Pluripotency and differentiation of embryonic stem cells.
- L. Studer, Memorial Sloan-Kettering Cancer Center, New

York: Human ES cell in neural development and repair.

- H. Niwa, RIKEN, Hyogo, Japan: Transcriptional regulation for self-renewal and differentiation of ES cells.
- H.R. Scholer, University of Pennsylvania, Kennett Square: Derivation of germ cells from mouse embryonic stem cells.

SESSION 2: Differentiation of Mes Endoderm
Chairperson: G. Keller, Mount Sinai School of Medicine, New York

- K. Zaret, Fox Chase Cancer Center, Philadelphia, Pennsylvania: Specification of liver and pancreas progenitors from the embryonic endoderm.
- H. Semb, Gothenburg University, Goteborg, Germany: Differentiation of human ES cells toward endoderm and pancreatic cell lineages.
- C. Mummery, Netherlands Institute for Developmental Biology, Utrecht: Cardiomyocyte differentiation of human ES cells.
- R. Jaenisch, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts: Reprogramming the genome.
- A. Wobus, Institute of Plant Genetics Gatersleben, Germany: ES cell differentiation into functional beta-like cells and the role of nestin expression.
- G. Keller, Mount Sinai School of Medicine, New York: Lineage induction and specification during embryonic stem cell differentiation.
- R. McKay, National Institute of Neurological Disorders and Stroke, NIH, Bethesda, Maryland: Deriving the cellular phenotype.



L. Zoloth, R. McKay

SESSION 3: Stem Cells in the Life Cycle

Chairperson: R.A. Pedersen, Addenbrooke's Hospital, Cambridge, United Kingdom

K. Hochedlinger, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts: Reprogramming of cancer cells by nuclear transfer.

P. Lanscorp, British Columbia Cancer Research Center, Vancouver: Telomerase and "self-renewal" of stem cells.

SESSION 4: What Is Ethically Possible?

Chairperson: R. McKay, National Institute of Neurological Disorders and Stroke, NIH, Bethesda, Maryland

L.S. Zoloth, Northwestern University, Chicago, Illinois: Ethical considerations in the organization of research in pluripotent cells.

SESSION 5: Implementing the Promise of Pluripotent Cells from Mouse to Man

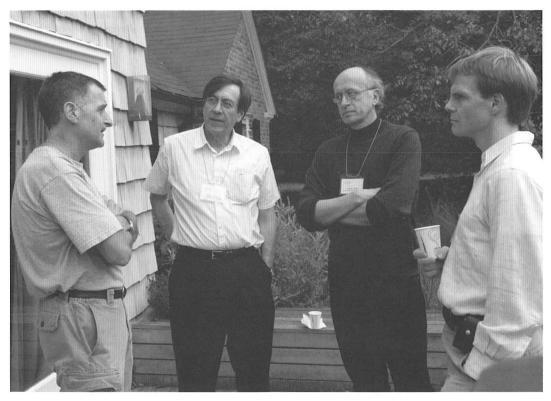
Chairperson: R. McKay, National Institute of Neurological Disorders and Stroke, NIH, Bethesda, Maryland

R.R. Behringer, M.D. Anderson Cancer Center, Houston, Texas: Genetic studies of early mouse development.

R.A. Pedersen, Addenbrooke's Hospital, Cambridge, United Kingdom: Taking human ES cells to the clinic.

H. Weber, Medical Research Council, London, United Kingdom: The United Kingdom Stem Cell Initiative.

J.F. Battey, National Institute on Deafness and Other Communication Disorders, NIH, Bethesda, Maryland: NIH support for human embryonic stem cell research.



J. Battey, R. Pedersen, G. Keller, L. Studer

Finding New Genes Linked to ALS: A Focus on Current Technologies and Their Potential Application

October 26-28

FUNDED BY

The ALS Association

ARRANGED BY

R.H. Brown, Massachusetts General Hospital, Charlestown L. Bruijn, The ALS Association, Guilford, Connecticut

SESSION 1: Opening Remarks

Chairperson: L. Bruijn, The ALS Association, Guilford, Connecticut

R.V. Abendroth, The ALS Association, Milwaukee, Wisconsin: Opening remarks.

R.H. Brown, Massachusetts General Hospital, Charlestown: Introduction to ALS and ALS genetics.

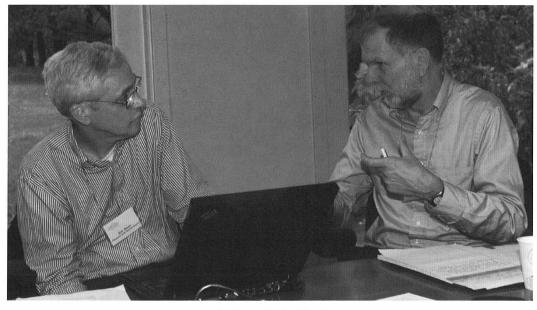
D. Altshuler, Massachusetts General Hospital, Boston: The challenge of complex genetics: Overview.

SESSION 2: Statistical Approaches to Complex Genetics
Chairperson: A. Al Chalabi, Institute of Psychiatry, London, United
Kingdom

E. Martin, Duke University Medical Center, Durham, North Carolina: Theoretical considerations: TDT, case control, other models.

D.B. Goldstein, University College London, United Kingdom: Approaches to haplotype reduction.

J. Haines, Vanderbilt University Medical Center, Nashville, Tennessee: Practical considerations: Size and power calculations.



R. Brown, K. Fischbeck

SESSION 3: Techniques

Chairperson: R. Baughman, National Institute of Neurological Disorders and Stroke, NIH, Bethesda, Maryland

D.R. Cox, Perlegen Sciences, Inc. Mountain View, California: Chip-based SNP analysis.

P.J. de Jong, Children's Hospital Oakland Research Institute, California: Cloning approaches toward the sequencing of disease haplotypes.

SESSION 4: Precedents in Complex Analyses of Human Diseases

Chairperson: J. Haines, Vanderbilt University Medical Center, Nashville, Tennessee

S. Hauser, University of California, San Francisco: Investigations of selected neurological disorders.

D. Goldman, National Institute on Alcohol Abuse &

Alcoholism, Rockville, Maryland: Genetic and functional analyses of serotonin transporter in affective disorders.

SESSION 5: Application of Complex Genetics to ALS **Chairpersons: R.H. Brown,** Massachusetts General Hospital, Charlestown, and **P.J. de Jong,** Children's Hospital Oakland Research Institute, California

L. Bruijn, The ALS Association, Guilford, Connecticut: The challenge.

 A. Al Chalabi, Institute of Psychiatry, London, United Kingdom: Complex genetics in ALS: Studies to date.
 G.A. Rouleau, Montreal General Hospital, Canada: How do we proceed?

Discussion

Moderators: K.H. Fischbeck, National Institute of Neurological Disorders and Stroke, NIH, Bethesda, Maryland, and G.A. Rouleau, Montreal General Hospital, Canada



D. Altshuler, D. Cox

Molecular Differentiation of Benign and Malignant Pheochromocytomas and Neuroblastomas

November 16-18

FUNDED BY

National Hypertension Association, Inc.

ARRANGED BY

G. Eisenhofer, National Institute of Neurological Disorders & Stroke, NIH, Bethesda, Maryland

W.M. Manger, National Hypertension Association, New York

Introductory Remarks and Summary of Expectations:

W.M. Manger, National Hypertension Association, New York

SESSION 1: Current Status of Diagnosis, Localization, Clinical Management, and Treatment **Chairperson: W.M. Manger,** National Hypertension Association, New York

D.S. Goldstein, National Institute of Neurological Disorders and Stroke, NIH, Bethesda, Maryland: Diagnostic markers of malignancy in pheochromocytoma: Issues for biochemical and imaging approaches.

W.F. Young, Mayo Clinic, Rochester, Minnesota: Management of malignant pheochromocytoma.

N.-K.V. Cheung, Memorial Sloan-Kettering Cancer Center, New York: Neuroblastoma: A clinical enigma.

B.L. Shulkin, University Hospital, Ann Arbor, Michigan: 131I-MIBG therapy and new radiopharmaceuticals for pheochromocytoma.

SESSION 2: Tumor Genetics

Chairperson: H. Lehnert, University of Magdeburg, Germany

D. Smith, Mayo Clinic, Rochester, Minnesota: Microarrays and advanced technologies for the study of cancer.

H.P.H. Neumann, Medizinische Universitatsklinik, Freiburg, Germany: Malignant pheochromocytoma: Role of genetic screening.

P. Dahia, Dana-Farber Cancer Institute, Boston, Massachusetts: The growing complexity of the genetics of pheochromocytoma.

J.M. Maris, Children's Hospital of Philadelphia, Pennsylvania: Genetic basis for neuroblastoma heterogeneity.

G. Eisenhofer, National Institute of Neurological Disorders and Stroke, NIH, Bethesda, Maryland: Distinct gene expression profiles in hereditary and sporadic pheochromocytoma.



SESSION 3: Malignant Pheochromocytoma

Chairperson: H.P.H. Neumann, Medizinische Universitatsklinik, Freiburg, Germany

- T.J. Giordano, University of Michigan Health System, Ann Arbor: Distinct transcriptional profiles of metastasizing and nonmetastasizing adrenal and extra-adrenal paragangliomas uncovered by DNA microarray analysis.
- H. Lehnert, University of Magdeburg, Germany: Expression patterns of the telomeric complex and somatostatin receptor subtypes in benign and malignant pheochromocytoma: Implications for diagnosis and treatment.
- R.R. de Krijger, Erasmus MC, Rotterdam, The Netherlands: Candidate gene and global genetic approaches to malignancy in pheochromocytoma.
- K. Pacak, National Institute of Neurological Disorders and Stroke, NIH, Bethesda, Maryland: Proteomics, microarrays, and model systems for improved diagnosis and treatment of malignant pheochromocytoma.

SESSION 4: Models, Pathways, and Mechanisms of Tumorigenesis Chairperson: S. Bornstein, University of Dusseldorf, Germany

- A. Tischler, New England Medical Center, Boston, Massachusetts: Experimental models of pheochromocytoma.
 L.A. Greene, Columbia University, New York: Regulation of pheochromocytoma differentiation and proliferation by ATF5.
- SESSION 5: Review of Presentations
- Chairpersons: G. Eisenhofer, National Institute of Neurological Disorders & Stroke, NIH, Bethesda, Maryland; W.M. Manger, National Hypertension Association, New York
- R. Lucito, Cold Spring Harbor Laboratory: High-resolution gene-copy-number detection using ROMA, representational oligonucleotide microarray analysis.
- SESSION 6: Open Discussion Session
 Moderator: S. Bornstein, University of Dusseldorf, Germany
- Topic 1: Prognostic Markers and Targets for Treatment H. Lehnert, University of Magdeburg, Germany A. Tischler, New England Medical Center, Boston, Massachusetts
- **Topic 2:** Gene Expression Profiling and Proteomics D. Smith, Mayo Clinic, Rochester, Minnesota

- A. lavarone, Columbia University, New York: The N-myc-ID2-Rb pathway in neuroblastoma.
- D. Yamashiro, Columbia University, New York: Angiogenic factors in neuroblastoma.
- Topic 3: Tissue Banks and Tissue Sharing
 T.J. Giordano, University of Michigan Health System, Ann Arbor
 P. Dahia, Dana-Farber Cancer Institute, Boston
 Massachusetts
- Topic 4: Tissue Procurement and Data Management
 F. Brouwers, National Institute of Child Health and Human
 Development, NIH, Bethesda, Maryland
- H.P.H. Neumann, Medizinische Universitat-sklinik, Freiburg, Germany
- Topic 5: Models
- A. Tischler, New England Medical Center, Boston, Massachusetts
- Topic 6: Pheochromocytoma Research Consortium K. Pacak, National Institute of Neurological Disorders & Stroke, NIH, Bethesda, Maryland
- Topic 7: Funding, Future Interactions, and Directions W.M. Manger, National Hypertension Association, New York G. Eisenhofer, National Institute of Neurological Disorders & Stroke, NIH, Bethesda, Maryland



G. Eisenhofer, R. Lucito, W. Manger

Neural Representation and Processing of Temporal Patterns

December 14-17

FUNDED BY

Redwood Neuroscience Institute

ARRANGED BY

C. Brody, Cold Spring Harbor Laboratory

D. Buonomano, University of California, Los Angeles

J.C. Hawkins, Redwood Neuroscience Institute, Menlo Park, California

SESSION 1

J.C. Hawkins, Redwood Neuroscience Institute, Menlo Park, California: Temporal processing: Questions and definitions. M.N. Shadlen, Howard Hughes Medical Institute, University

of Washington, Seattle: Representation of elapsed time and hazard rates in parietal cortex of the macaque.

P.A. Tallal, Rutgers University, Newark, New Jersey: Neural

signature of rapid auditory processing disorders in dyslexia: Insights from fMRI and remediation studies,

C. Brody, Cold Spring Harbor Laboratory: Timing and the neural representation of short-term memories.

X.-J. Wang, Brandeis University, Waltham, Massachusetts: A biophysical model of robust scalar timing.

SESSION 2

D. Buonomano, University of California, Los Angeles:
 Psychophysical and theoretical studies of simple and complex temporal processing.

M.P. Kilgard, University of Texas, Dallas: Temporal coding and plasticity in auditory cortex.

J.J. Hopfield, Princeton University, New Jersey: Encoding/

recognizing short dynamic trajectories: Audition.

E. Ahissar, The Weizmann Institute, Rehovot, Israel: Temporal encoding and decoding in vibrissal active touch.

J.C. Hawkins, Redwood Neuroscience Institute, Menlo Park, California: Time, sequences, and movement in perception.



M. Kilgard, P. Tallal

SESSION 3

- R. Ivry, University of California, Berkeley: The cerebellum and event timing.
- M.D. Mauk, University of Texas, Houston Medical School: Timing in the cerebellum.
- M. Fee, Bell Laboratories, Murray Hill, New Jersey: Neural representation of time in the songbird.
- W.H. Meck, Duke University, Durham, North Carolina: Coincidence-detection models of interval timing.
- R. Gallistel, University of California, Los Angeles: The temporal information content of a protocol as a determinant of acquisition latency.

SESSION 4

- S. Hooper, Ohio University, Athens: Temporal processing by single neurons.
- P. Verschure, Institute of Neuroinformatics, Zurich, Switzerland: Decoding information in a temporal pattern code.
- R. Granger, University of California, Irvine: Derivation and analysis of sequential processing algorithms in thalamocortical circuitry.
- T. Rammsayer, University of Goettingen, Germany: Neuropharmacological dissociation of distinct timing mechanisms in the brain.
- D.L. Harrington, Veterans Affairs Medical Center,
 Albuquerque, New Mexico: Neural representation of interval encoding and decision making.

SESSION 5

- D. Levitin, McGill University, Montreal, Canada: Temporal coherence in music and the prefrontal cortex.
- M.R. Jones, Ohio State University, Columbus: The dynamics of attending to auditory events.
- B.H. Repp, Haskins Laboratories, New Haven, Connecticut: Accentuation and coordination.
- A. Kepecs, Cold Spring Harbor Laboratory: A model of dynamics of graded persistent activity.



M. Jones, J. Hopfield

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Grantor	Program/Principal Investigator	Duration of Grant	2003 Funding+
FEDERAL SUPPORT			
Brookhaven National Laboratory	Scientific Opportunities in Macromolecular Crystallography at NSLS-II	2003	\$ 5,256*
Centers for Disease Control and Prevention (CDC)	Toward Understanding the Cellular and Molecular Mechanisms of Medically Unexplained Fatigue	2003	22,000*
NIH	Quantitative Genetic Networks	2003	25,000*
NIH-National Human Genome Research Institute	Eugenics, Genes, and Human Behavior	2003	23,202
NIH-National Institute of Mental Health (through a grant to FRAXA Research Foundation)	Synaptic Function in Fragile-X	2003	32,848*
NONFEDERAL SUPPORT			
Meeting Support			
Affymetrix, Inc.	Taking Cancer Genomics to the Clinic	2003	37,280°
The ALS Association	Finding New Genes Linked to Amyotrophic Lateral Sclerosis: A Focus on Current Technologies and Their Potential Application	2003	17,809°
Burroughs Wellcome Fund	Toward a More Unified Understanding of Infectious Disease	2003	30,847
CFIDS Association of America	Toward Understanding the Cellular and Molecular Mechanisms of Medically Unexplained Fatigue	2003	5,000*
National Hypertension Association	Molecular Differentiation of Benign and Malignant Pheochromocytomas and Neuroblastomas	2003	3,760*
Redwood Neuroscience Institute	Neural Representation and Processing of Temporal Patterns	2003	41,632*
Albert B. Sabin Vaccine Institute, Inc.	Feasible Solutions to Global Vaccine Shortages	2003	33,595*
Alfred P. Sloan Foundation	Taxonomy and DNA Taxonomy, DNA, and the Bar Code of Life	2003	37,500*
The Swartz Foundation	Neural Circuits: Principles of Design and Operation	2003	42,632*
Verto Institute, LLC	The Biology of Neuroendocrine Tumors	2003	28,798*

^{*}New grants awarded in 2003.

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