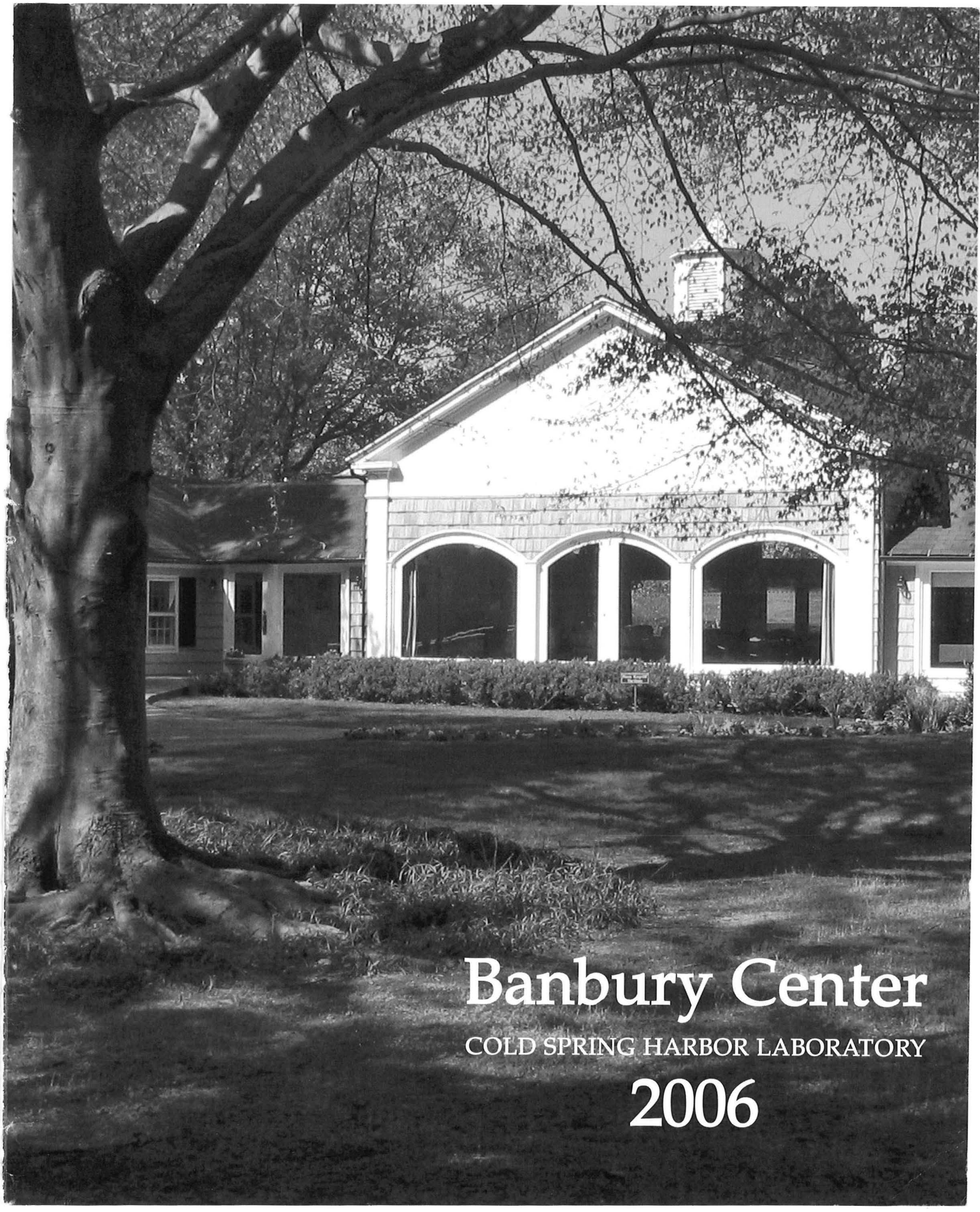

# Banbury Center

COLD SPRING HARBOR LABORATORY

2006

# 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. On-site 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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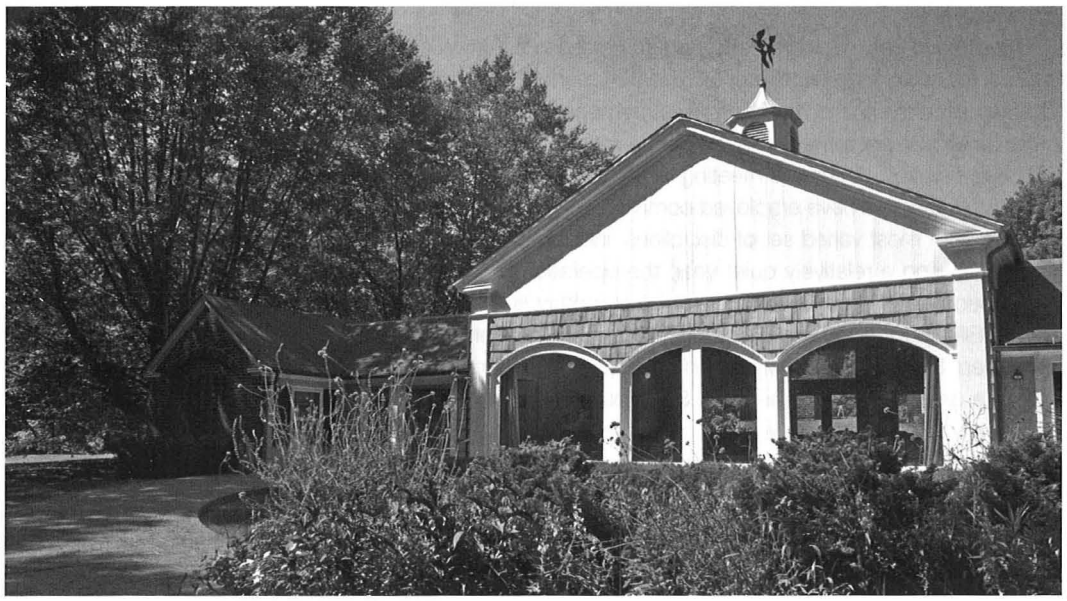
# BANBURY CENTER
# EXECUTIVE DIRECTOR'S REPORT

The Banbury Center Annual Report has followed the same format since the first Annual Report in 1976 (although the 1976 report was only 2 pages long compared with the 52-page 2005 report!). This year, however, the format has changed. Instead of a long introductory director's report describing the meetings, followed by the individual programs, a short description of each meeting now precedes its program.

Banbury Center continues to have a very full schedule of meetings. Even though 2006 was relatively quiet compared with the record-breaking year 2005, we nevertheless held 17 scientific meetings, a typical number. Of the 607 scientists who attended the scientific meetings, 82% came from the United States, a proportion that has remained remarkably constant in recent years. These participants came from 35 states, with California, Maryland, Massachusetts, and New York providing 45% of the total number of participants. One hundred fourteen scientists from 19 countries participated in meetings, for a total of 114. Canada, France, Germany, Sweden, and the United Kingdom provided more than 50% of these scientists. In addition, the Center was used for 15 other events, including six courses, group meetings for Laboratory scientists, two week-long courses for the Watson School of Biological Sciences, and two meetings for local nonprofit groups. Altogether, there were 32 events here in 2006.

The distribution of topics was similar to that previous years, although most of the meetings dealt with neurological and mental disorders. This reflects the intrinsic importance of these topics and the Laboratory's increasing research interest in these areas. Two meetings were held on the genetics of mental disorders (autism and bipolar disorder) and four on degenerative disorders where considerable progress has been made in understanding their molecular pathogenesis (fragile-X syndrome, spinal muscular atrophy, Parkinson's disease, and amyotrophic lateral sclerosis). In addition, neuroscience was the focus of three meetings. One reviewed the experimental analysis of neurogenesis in the adult brain, a topic of critical importance if therapies are to be developed for stroke and other forms of brain trauma. Another dealth with memory and whether recalled memories are "labile" and subject to modification before being "reconsolidated." This phenomenon may be important in assessing the validity of "recovered memories." One meeting reviewed the interactions between physiological and psychological correlates of feeding and appetite. This meeting followed up on a Banbury Center meeting in 1998



Banbury Center conference room, summer

Banbury Center conference room, winter

on obesity. At that time, leptin had just been identified and that meeting was concerned with what had been learned of the physiological basis of obesity.

There were two meetings relating to infectious diseases. The meeting on Lyme disease, one of a long series of Banbury Center meetings on the topic, reviewed the controversial issue of "chronic" Lyme disease, that is, the persistence of Lyme-disease-like symptoms in the absence of infection. The second meeting discussed the latest findings on innate, as opposed to acquired, immunity. This, it seems, is found in all multicellular organisms, and a notable feature of the meeting was that the participants worked on plants, invertebrates, and vertebrates.

The meeting on innate immunity included plants, but the Banbury plant meeting itself discussed the integration of hormonal and genetic regulation of plant development. These have been regarded as separate fields of research, but it has become clear that the two broad developmental pathways are closely linked. Participants examined the extent to which hormones regulate known genetic pathways and vice versa.

There have been repeated attempts to establish a theoretical biology that would provide a firm conceptual framework for experimental research, performing a role analogous to that of theoretical physics. Theoretical analysis and modeling have, perhaps, played a greater role in neuroscience research than in other biological disciplines, and we held a meeting that reviewed computational approaches to modeling brain function. A second meeting dealt with more general features of biological systems, examining whether organisms have employed common engineering principles in their evolution. It drew on participants from a most varied set of disciplines, including mathematics, engineering theory, and biology.

Even during a relatively quiet year, the operation of Banbury Center still requires a major effort by many people. That our meetings run so smoothly is a tribute to the hard work of Sydney Gary, Bea Toliver, Ellie Sidorenko, and Barbara Polakowski. The Center's grounds crew staff Mike Peluso and Joe Ellis keep the Banbury environment a beautiful resource for our participants. Our hectic schedule places a great burden on the Food Services and Housekeeping departments whose staffs must cope with ever-changing schedules and rapid turnarounds. I thank all of these people and the scientists at the Laboratory who continue to support the Banbury Center activities.

**Jan Witkowski**
*Executive Director*

# MEETINGS

## The Evolving Role of the Board-certified Medical Geneticist

**February 14–16**

FUNDED BY **American College of Medical Genetics and individual participants**

ARRANGED BY **B.R. Korf,** University of Alabama, Birmingham

### BACKGROUND

As a result of the advances in gene mapping using, for example, single-nucleotide polymorphisms (SNPs) and genome-wide tools such as microarrays, we now know the genes underlying some 2000 human inherited disorders. However, despite this dramatic increase in our ability to use molecular techniques for diagnosis, applications of this knowledge have been limited. This discussion meeting focused on defining the role of the medical geneticist in rare and common disorders.

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

**SESSION 1:** Setting the Stage

B.R. Korf, University of Alabama, Birmingham
D.H. Ledbetter, Emory University School of Medicine, Atlanta, Georgia
M.F. Murray, Harvard Medical School, Boston, Massachusetts: Welcome and overview of meeting.
J. Zonana, University of Oregon Health Science University, Portland: Roles of medical geneticists outside of the United States.
G. Feldman, Wayne State University, Detroit, Michigan: Roles of medical geneticists in the United States.
R. Bachman, Kaiser Permanente Hospital, Oakland, California: Genetic services: The HMO model.
M. Blitzer, University of Maryland: Genetic workforce study.

**SESSION 2:** Role of the Medical Geneticist

B.R. Korf, University of Alabama, Birmingham: Pediatrics.
M.F. Murray, Harvard Medical School, Boston, Massachusetts: Adult medicine.
J.L. Simpson, Baylor College of Medicine, Houston, Texas: Prenatal diagnosis.
M. Scheuner, RAND Corporation, Santa Monica, California: Public health.

**General Discussion:** Action items and planned follow-up

# Research on Genetics of Bipolar Disorder: Current Approaches and Future Directions

**February 22**

FUNDED BY **The Stanley Foundation**

ARRANGED BY **J.D. Watson,** Cold Spring Harbor Laboratory
**S. Gary,** Banbury Center, Cold Spring Harbor Laboratory

## BACKGROUND

This discussion meeting was held to assess the current state of research on bipolar disorder. As with many psychiatric disorders, research on the genetics of bipolar disorder has been slow to identify genes underlying the condition. Many factors contribute to this lack of progress, including the heterogeneity of the disorder and the absence of a definitive diagnostic classification scheme. The meeting focused on genetic approaches, and participants reviewed lessons learned from past collaborative efforts and discussed what is needed to establish a new collaborative project. The meeting concluded with a discussion on future experiments and the importance of sharing resources and data.

**Welcome: J.D. Watson,** Cold Spring Harbor Laboratory

J.R. DePaulo and J. Potash, Johns Hopkins University School of Medicine, Baltimore, Maryland: Overview of clinical aspects of bipolar disorder.

E.S. Gershon, University of Chicago, Illinois: Current status of research on genetics of bipolar disorder.

J. Sebat, Cold Spring Harbor Laboratory: ROMA analysis of autism.

**Discussion of Future Research Directions**

**Questions for discussion**

What patient groups are currently represented in the available DNA collections?

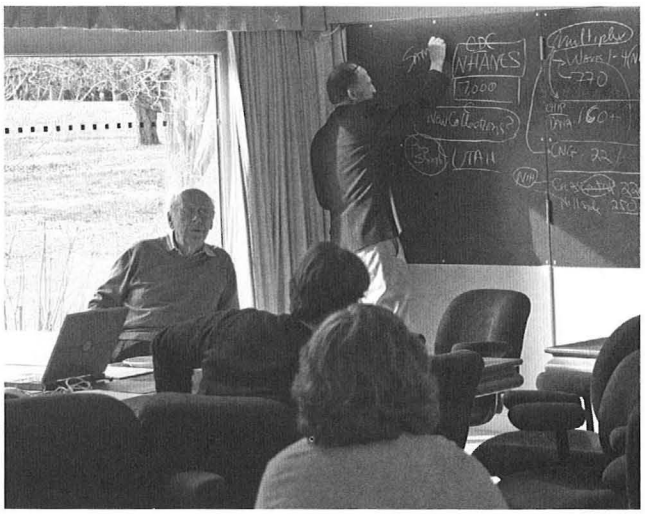
What information is important in collecting future samples?

What are the concerns and suggestions regarding overlap between bipolar and schizophrenia?

Limit analysis to sib pairs? Other approaches?

Future directions? How best to proceed?

A. Malhotra, T. Marr, E. Gershon




J. Watson, R. DePaulo

# Neurogenesis in the Adult Brain

**February 26–March 1**

FUNDED BY **Cold Spring Harbor Laboratory Corporate Sponsor Program**

ARRANGED BY **F. H. Gage,** The Salk Institute for Biological Studies, San Diego, California
**G. Enikolopov,** Cold Spring Harbor Laboratory

**BACKGROUND**

Research efforts on neurogenesis in the adult brain have grown substantially in recent years. Improved methods allow researchers to observe the birth and function of new neurons in the adult, leading to some exciting reports on the role of neurogenesis not only in the normal adult brain, but also in certain neurological disorders such as depression and stroke. This meeting examined such questions as What are the molecular and morphological characteristics of the cells as they transition from stem cells to mature neurons? What are the key molecular, cellular and electrophysiological mechanisms that regulate different aspects of the maturation process? Are changes in neurogenesis responsible for disease-related changes in behavior?

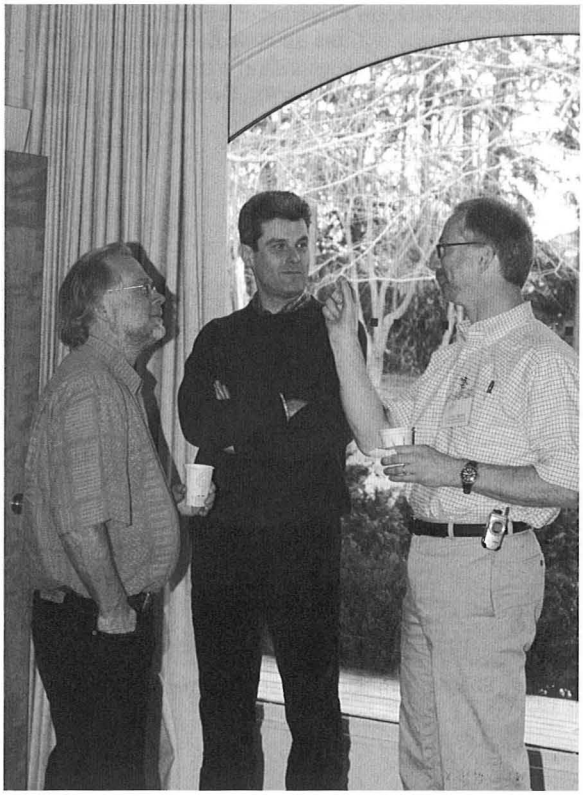
**Introduction:** **S. Gary,** Banbury Center, Cold Spring Harbor Laboratory
**F.H. Gage,** The Salk Institute for Biological Studies, San Diego, California

**SESSION 1:** Basic Processes of Adult Neurogenesis
**Chairperson: J.D. Macklis,** Harvard Medical Center, Boston, Massachusetts

D. Van Der Kooy, University of Toronto, Ontario, Canada: The origin of adult neurons from stem and progenitor cells.
G. Enikolopov, Cold Spring Harbor Laboratory: Differentiation cascade in the hippocampus.
C. Lie, Institute for Developmental Genetics, Munich, Germany: Role of Wnt signaling in hippocampal neurogenesis.
A. Schinder, Leloir Institute Foundation, Buenos Aires, Argentina: Functional convergence of neurons generated in the developing and adult hippocampus.

**SESSION 2:** Molecular Mechanisms Regulating Neurogenesis
**Chairperson: R. McKay,** National Institute of Neurological Disorders and Stroke/NIH, Bethesda, Maryland

F. Doetsch, Columbia University, New York: MicroRNA regulation of adult neurogenesis.
H.G. Kuhn, Goteburg University, Sweden: Peripheral growth factors as stimulants for adult neurogenesis.
J. Bischofberger, Physiologisches Institut der Universitat Freiburg, Germany: Calcium signaling and synaptic plasticity in newly generated hippocampal granule cells.
H. Song, Johns Hopkins University School of Medicine, Baltimore, Maryland: Molecular mechanisms regulating synaptic integration and plasticity of newly generated neurons in the adult brain.
D.A. Steindler, University of Florida Brain Institute, Gainesville: Tying together cell and molecular interactions that regulate neurogenesis.



R. Hen, G. Kempermann, J. Macklis

**SESSION 3:** Regulation of Adult Neurogenesis
**Chairperson: P. Rakic,** Yale University School of Medicine, New Haven, Connecticut

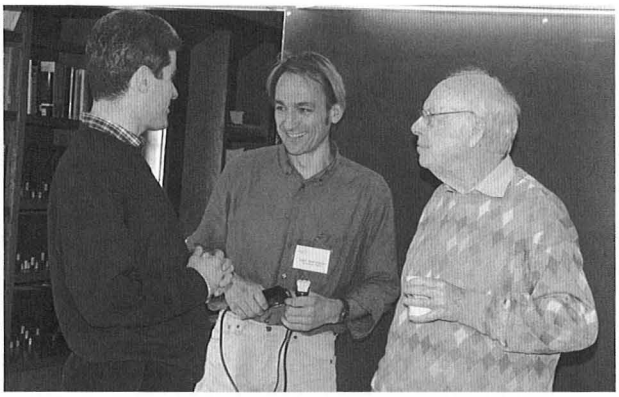
G. Kempermann, Max Delbrück Center for Molecular Medicine, Berlin, Germany: Natural variation and genetic covariance in adult hippocampal neurogenesis.
H. van Praag, Salk Institute for Biological Studies, San Diego, California: Regulation of neurogenesis by exercise in rodents.
H.A. Cameron, National Institute of Mental Health/NIH, Bethesda, Maryland: Regulation of new neuron survival by learning.
S.A. Small, Columbia University, New York: MRI correlates of neurogenesis in mice and humans.
D.N. Abrous, Institute Francois Magendie, Bordeaux, France: Comments and discussion on "environmental regulation of adult neurogenesis."

**SESSION 4:** Functional Significance of Adult Neurogenesis
**Chairperson: F.H. Gage,** The Salk Institute for Biological Studies, San Diego, California

R. Hen, Columbia University, New York: Hippocampal neurogenesis contributes to contextual fear learning and antidepressant response.
T.J. Shors, Rutgers University, Piscataway, New Jersey: Learning and neurogenesis: What is it about learning that rescues new neurons from death?
J.M. Wojtowicz, University of Toronto, Ontario, Canada: Radiation-induced inhibition of neurogenesis interferes with hippocampus-dependent memory function.
S. Jessberger, The Salk Institute for Biological Studies, La Jolla, California: Aberrant neurogenesis contributes to cognitive impairment following seizure activity.

**SESSION 5:** Role for Neurogenesis in Disease
**Chairperson: P. Eriksson,** Sahlgrenska Academy Goteburg University, Sweden

R.S. Duman, Yale University School of Medicine, New Haven, Connecticut: Neurogenic actions of antidepressants.
A. Pieper, University of Texas Southwestern Medical Center, Dallas: NPAS3 and neurogenesis in schizophrenia.
O. Lindvall, Lund University Hospital, Sweden: Neurogenesis after ischemic and epileptic insults in adult brain.
S.A. Goldman, The University of Rochester Medical Center, New York: Hb9 enhancer-based isolation and targeting of human motor neurons.



G. Kempermann, J. Bischofberger, J. Watson

S. Jessberger, F. Gage

# A Critical Assessment of Autism Genetics

**March 12–15**

FUNDED BY **Autism Speaks; Cure Autism Now; McLaughlin Centre for Molecular Medicine; Nancy Lurie Marks Family Foundation; National Alliance for Autism Research; Simons Foundation**

ARRANGED BY **A.P. Monaco,** University of Oxford, United Kingdom
**S.W. Scherer,** The Hospital for Sick Children, Toronto, Canada
**A.J. Bailey,** University of Oxford, United Kingdom

## BACKGROUND

Autism is known to have a strong genetic etiology, but even after many years of molecular genetic studies, it has been difficult to identify susceptibility genes for autism that are influencing a large majority of patients. However, there is increasing optimism that this is about to change. The new tools of genomics that, for example, enable high-density genetic marker studies of individual regions and the whole genome at reasonable cost, combined with larger families being studied, will hopefully yield new data. Participants in the meeting critically assessed the current state of research and looked for the leads that should be followed in the future.

**Introduction:** **S. Gary,** Banbury Center, Cold Spring Harbor Laboratory

**SESSION 1:** Clinical Aspects
**Chairperson: A.P. Monaco,** University of Oxford, United Kingdom

P. Szatmari, McMaster University, Ontario, Canada: Historical and clinical introduction.
A.J. Bailey, University of Oxford, United Kingdom: Utilizing the whole autism phenotype.
S. Baron-Cohen, University of Cambridge, United Kingdom: Hypersystemizing, assortative mating, and androgens.
D. Skuse, Institute of Child Health, London, United Kingdom: Potential X-linked mechanisms influencing susceptibility to autistic traits.
E. Fombonne, Montreal Children's Hospital, Canada: Recent trends in the epidemiology of autism and hypotheses about environmental exposures.

**Key Points and Discussion: P. Szatmari,** McMaster University, Ontario, Canada

**SESSION 2:** Whole-genome Genetic Studies
**Chairperson: S.W. Scherer,** The Hospital for Sick Children, Toronto, Canada

V.J. Vieland, University of Iowa, Iowa City: The incredible shrinking LOD: How increasing the sample size can actually obscure true linkage peaks, and what we can do about this.
D. Geschwind, University of California School of Medicine, Los Angeles: Approaching heterogeneity in autism: Endophenotypes and candidate pathway analysis.
I. Jarvela, University of Helsinki, Finland: Molecular genetics of Asperger syndrome, the under-diagnosed endophenotype among autism spectrum disorders.
J. Lamb, University of Oxford, United Kingdom: Gender and parent of origin affects in linkage data from IMGSAC.
G.D. Schellenberg, Seattle V.A. Medical Center, Washington: Recently completed genome scan of 225 families.
A. Chakravarti, Johns Hopkins University School of Medicine, Baltimore, Maryland: A linkage and association scan for autism genes.

**Key Points and Discussion: M.A. Pericak-Vance,** Duke University Medical Center, Durham, North Carolina

**SESSION 3:** Candidate Genes and Regional Association Studies
**Chairperson: A.J. Bailey,** University of Oxford, United Kingdom

J. Sutcliffe, Vanderbilt University, Nashville, Tennessee: Autism susceptibility and dysregulation of serotonin.
J. Lamb, University of Oxford, United Kingdom, and E. Maestrini, University of Bologna, Italy: A high-density SNP association study of the autism susceptibility loci on chromosomes 2q24-q32 and 7q21-q33.
J. Buxbaum, Mt. Sinai School of Medicine, New York: Chromosome 2q in autism.
A.L. Beaudet, Baylor College of Medicine, Houston, Texas: A mixed genetic and epigenetic, and mixed de novo and inherited model for autism.
T. Bourgeron, Institut Pasteur, Paris, France: Autism spectrum disorders and synaptic plasticity.

**Key Points and Discussion: M. Gill,** St. James' Hospital, Dublin, Ireland

**SESSION 4:** Chromosomal Abnormalities/Copy-number Variants
**Chairperson: M.A. Pericak-Vance,** Duke University Medical Center, Durham, North Carolina

C. Lee, Brigham and Women's Hospital, Boston, Massachusetts: Array-based comparative genomic hybridization and copy-number variation in the human genome.
J. Sebat, Cold Spring Harbor Laboratory: A high-resolution scan for genome copy-number variation in autism.
E.E. Eichler, University of Washington, Seattle: Structural variation, mental retardation, and autism.
S.W. Scherer, The Hospital for Sick Children, Toronto, Canada: Cytogenomic investigations into the molecular etiology of autistic spectrum disorder.
N.C. Schanen, University of Delaware, Wilmington: Autism spectrum disorders in duplication chromosome 15 syndrome.
S. Muthuswamy, Cold Spring Harbor Laboratory: CNP allelic imbalance in autism.

**Key points and discussion: G.D. Schellenberg,** Seattle V.A. Medical Center, Washington

**SESSION 5:** Statistical Genetics
**Chairperson: V.J. Vieland,** University of Iowa, Iowa City

B. Devlin, University of Pittsburgh School of Medicine, Pennsylvania: Linkage genome scan for the autism genome project.
R.M. Cantor, University of California School of Medicine, Los Angeles: Evidence of gene on 17q contributing to autism in males.
E.M. Wijsman, University of Washington School of Medicine, Seattle: Multilocus models and analysis of component phenotypes.
M. Daly, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts: Genome-wide association prospects in the face of the great genetic complexity of autism.

**Key points and discussion: J.L. Haines,** Vanderbilt University Medical Center, Nashville, Tennessee

**Summary: A.P. Monaco,** University of Oxford, United Kingdom

# The Phenomenology of Reconsolidation

**March 26–29**

FUNDED BY **Volkswagen Foundation and Marie Robertson Memorial Fund**

ARRANGED BY **Y. Dudai,** Weizmann Institute of Science, Rehovot, Israel
**B. Everitt,** University of Cambridge, United Kingdom
**K. Nader,** McGill University, Montreal, Canada

**BACKGROUND**

We would all like to know more about our memories. How is it that our brains retain just a few memories out of the myriad events that we experience each moment of the day, and how is it that some of these memories are kept for decades? It seems that newly formed memory remains in a dynamic or "labile" form for a short time after which the memory trace is stabilized or "consolidated." During the past several years, it has emerged that after a memory undergoes consolidation, it may return to a labile state under certain circumstances, requiring it to be reconsolidated. There are important theoretical and practical implications of these findings, for example, with respect to a variety of mental illnesses, such as posttraumatic stress disorder, phobia, and drug addiction.

**Welcome: S. Gary,** Banbury Center, Cold Spring Harbor Laboratory

**History of the Phenomenon: S.J. Sara,** Université Pierre & Marie Curie, Paris, France

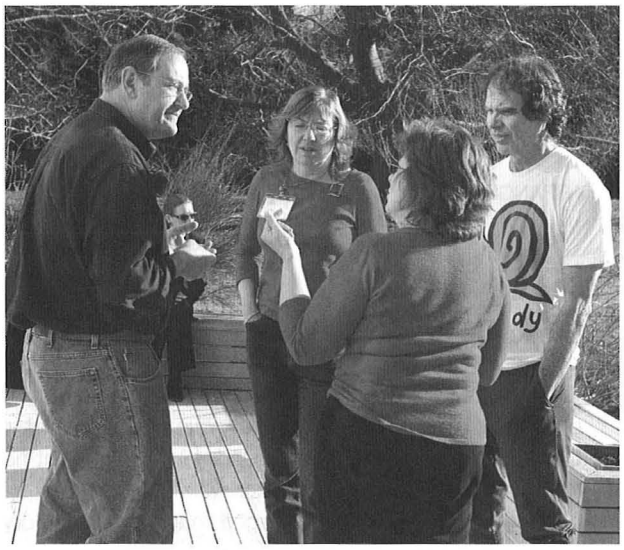
**SESSION 1:** The Nature of Amnesia
**Chairperson: S.J. Sara,** Université Pierre & Marie Curie, Paris, France

**Topic 1:** Why isn't there a resolution to the nature of amnesia? What are the issues?

D. Riccio, Kent State University, Ohio: Reconsolidation: A bit of history, a bit of (contrarian?) theory.
P.E. Gold, University of Illinois, Urbana-Champaign: Memories and amnesias.

**Topic 2:** New empirical approaches to the issue

L. de Hoz, Medical University Charite, Berlin, Germany: Memory loss and reminding in the spatial domain.
O. Hardt, University of Arizona, Tucson: A novel approach to identifying the nature of amnesia.



P. Gold, C. Rankin, S. Sara, K. Lukowiak

**SESSION 2:** Boundary Conditions on Reconsolidation and Other New Findings
**Chairperson: M. Walker,** Harvard Medical School, Boston, Massachusetts

**Brief Presentations**
Extinction
Strength of Training
Directly Reactivated versus Indirectly Reactivated Memories
Age of Memories
New Findings in Reconsolidation

**SESSION 3:** Reconsolidation Across Species and Tasks
**Chairperson: K.P. Giese,** University College of London, United Kingdom

M. Walker, Harvard Medical School, Boston, Massachusetts: Role of sleep in memory consolidation and reconsolidation.
S. Davis, CNRS and University Paris Sud, France: Cellular and molecular mechanisms of consolidation and reconsolidation.
B.W. Balleine, University of California, Los Angeles: Reconsolidation of appetitive memories.
K. Lukowiak, University of Calgary, Alberta, Canada: Reconsolidation and a well-rehearsed memory.
K. Anokhin, Russian Academy of Medical Sciences, Moscow: Reconsolidation and memory recovery in mice and chicks: A comparative perspective.

**SESSION 4:** Molecular and Cellular Mechanisms
**Chairperson: B.S. Everitt,** University of Cambridge, United Kingdom

R. Fonseca, Julio de Matos Hospital, Lisbon, Portugal: Neuronal activity determines the protein synthesis dependence of L-LTP.
C. Rankin, University of British Columbia, Vancouver, Canada: Blocking memory reconsolidation in *C. elegans* reverses behavioral expression of memory as well as establishes changes in glutamate receptor expression.
S. Kida, Tokyo University of Agriculture, Japan: Mechanisms of interaction between memory reconsolidation and extinction.
K.P. Giese, University College of London, United Kingdom: Reconsolidation as partial recapitulation of consolidation.
J.L.C. Lee, University of Cambridge, United Kingdom: The molecular mechanisms of fear memory consolidation and reconsolidation are doubly dissociable.
C. Albernini, Mt. Sinai School of Medicine, New York: Why does memory undergo reconsolidation? A working hypothesis from studies on inhibitory avoidance memory.
K. Nader, McGill University, Quebec, Canada: A neural manifestation of the overtraining boundary conditions on reconsolidation.

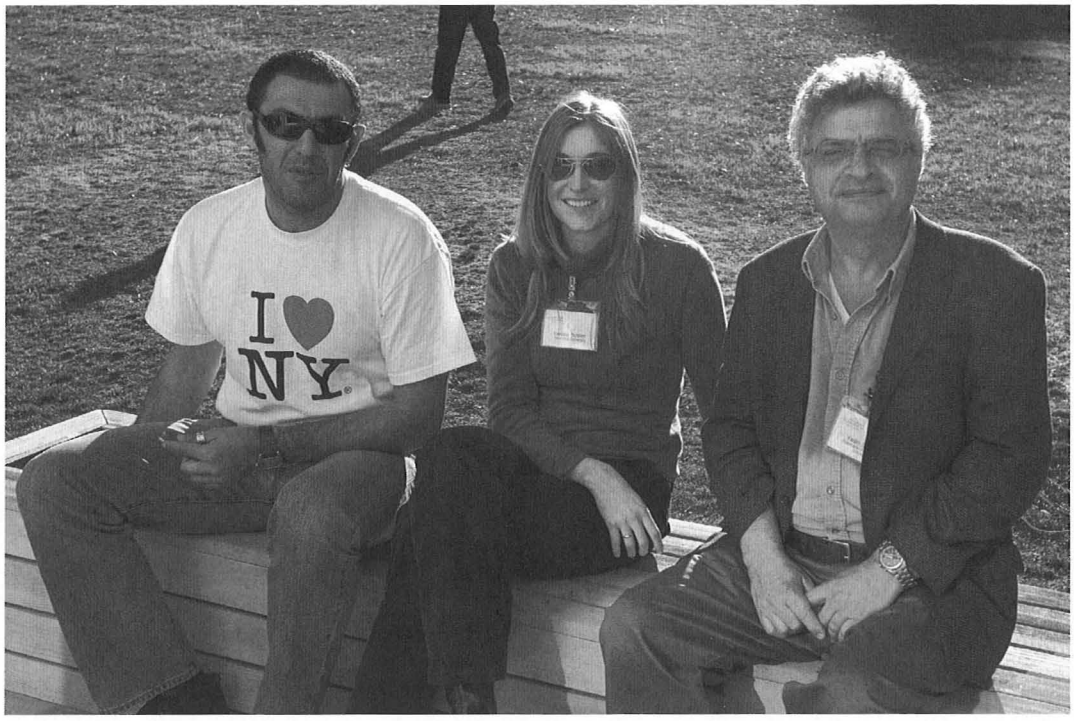
**SESSION 5:** Reconsolidation in Normal and Psychopathological Memories
**Chairperson: L. Nadel,** University of Arizona, Tucson

S.J. Sara, Universite Pierre and Marie Curie, Paris, France: Learning-related activation of locus coeruleus during slow wave sleep: A new player on the reactivation scene?
M. Altemus, Cornell University, New York: Fear conditioning in healthy humans: Effects of propranolol.
J. Gorman, McLean Hospital, Belmont, Massachusetts: The significance of reconsolidation of fear memories for the treatment of anxiety disorders.
E. Phelps, New York University: Reconsolidation in humans? Specific challenges.
R.K. Pitman, Harvard Medical School, Charlestown, Massachusetts: Translational model of PTSD updated: Role of reconsolidation and treatment implications.
K. Myers, Emory University, Atlanta, Georgia: Extinction shortly following fear acquisition may erase conditioned fear.
B.S. Everitt, University of Cambridge, United Kingdom: Memory reconsolidation as a therapeutic target in drug addiction.

**SESSION 6:** Interpretations and New Directions
**Chairperson: B.S. Everitt,** University of Cambridge, United Kingdom

L. Nadel, University of Arizona, Tucson: Reconsolidation: Challenging fundamental concepts of memory.
Y. Dudai, The Weizmann Institute of Science, Rehovot, Israel: Reconsolidation: Taping into trace persistence and use.

**Group Discussion**
**Mediator: Y. Dudai,** The Weizmann Institute of Science, Rehovot, Israel




N. Nader, D. Schiller, Y. Dudai

# Computational Approaches to Cortical Functions

**April 2–5**

FUNDED BY **The Swartz Foundation**

ARRANGED BY **L.F. Abbott,** Columbia University, New York
**H. Cohen,** The Swartz Foundation, Scarborough, New York
**R.M. Shapley,** New York University

## BACKGROUND

The meeting focused on the dynamics of large-scale computational models of the cerebral cortex, including both theoretical and experimental results concerning large-scale neural systems. Participants discussed modeling requirements at the synaptic, neuronal, and circuit levels, as well as the effects of network size and scaling rules. Other topics covered included propagation and gating of signals, self-sustained oscillations and reverberatory states, spike and local field relationships, chaotic activity, and other phenomena exhibited by these models and their experimental counterparts.

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

## SESSION 1

X.-J. Wang, Brandeis University, Waltham, Massachusetts: Neural mechanisms of feature-based attention in a two-network model of sensory processing.

W. Maass, Technical University of Graz, Austria: A model for computation in cortical microcircuits.

O. White, Massachusetts Institute of Technology, Cambridge: Signal reconstruction from recurrent neuronal networks.

K. Rajan, College of Physicians & Surgeons, New York: Controlling neural networks dynamics.

A. Aersten, Albert Ludwigs Universitat, Freiburg, Germany: Variability and precision in cortical networks.

**SESSION 2**

C. Geisler, Rutgers University, Newark, New Jersey: Behavior-dependent phase rescaling of hippocampal pyramidal cells.
T. Vogels, Columbia University, New York: Signal propagation and switching in networks.
M. Diesmann, Albert-Ludwigs University, Freiburg, Germany: Spike-timing-dependent plasticity in balanced random networks.
B. Pesaran, New York University: Free choice increases synaptic interactions between frontal and parietal cortex.
R. Yuste, Columbia University, New York: Internal dynamics determine the cortical response to thalamic stimulation.

**SESSION 3**

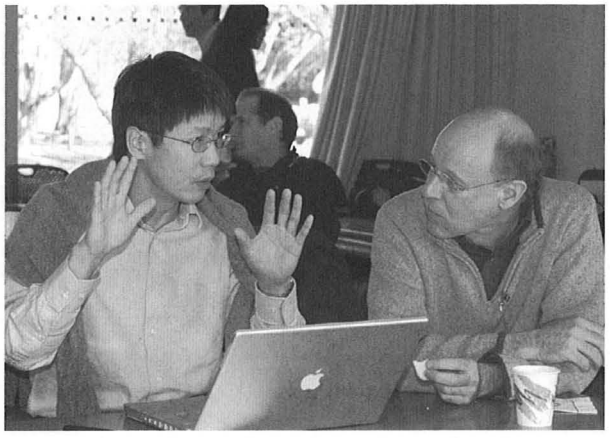
D. Cai, New York University: Spontaneous cortical activity in V1.
M.V. Tsodyks, Weizmann Institute of Science, Rehovot, Israel: Information encoding and processing via spatiotemporal patterns in cortical networks.
C. van Vreeswijk, Rene Descartes University, Paris, France: Role of dendritic shunting inhibition.
W. Gerstner, Ecole Polytechnique Federale de Lausanne, Switzerland: Ultra-short-term information buffering in a random network of spiking neurons: Macroscopic versus microscopic effects.
B. Knight, The Rockefeller University, New York: Neuron population dynamics in a simple canonical form.

**SESSION 4**

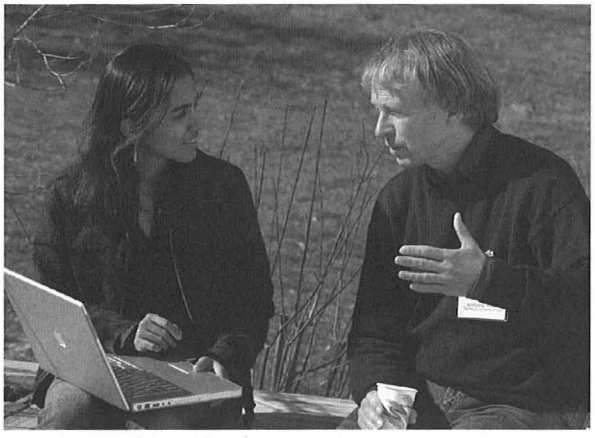
D. Tranchina, New York University: Try to save computation time in large-scale neural network modeling with population density methods, or just fuhgeddaboudit?
R.D. Traub, SUNY Downstate Medical Center, Brooklyn, New York: Gap junctions and fast oscillations in hippocampus and neocortex.
R.M. Shapiro, Cape Visions, Inc. New York, New York: Integrate and fire neural network: VLSI chip design.
A. Henrie, University of California, Los Angeles: Coherence of activity in primate V1.
D. Plenz, National Institute of Mental Health/NIH, Bethesda, Maryland: Neuronal avalanches in superficial layers of neocortex.

**SESSION 5**

M.J. Shelley, New York University: V1 dynamics and sparsity and multiple feature maps.
B. Murphy, University of California, San Francisco: Spontaneous activity and orientation maps in balanced cortical networks with structured V1-like connectivity.
A. Rangan, New York University: Cortical correlates underlying the line-motion-illusion phenomenon in primary visual cortex.
T. Thiagarajan, National Institute of Mental Health/NIH, Bethesda, Maryland: Precise propagation of initial neuronal group activity in neuronal avalanches in cortex.



X.-Y. Wang, L. Abbot



L. Rajan, W. Maas

# Fragile-X Syndrome: Basic Mechanisms and Treatment Implications

**April 9–12**

FUNDED BY **NIH–National Institute of Mental Health (through a grant to the University of Illinois)**

ARRANGED BY **W.T. Greenough,** University of Illinois, Urbana
**B.A. Oostra,** Erasmus Universiteit Rotterdam, The Netherlands
**E. Berry-Kravis,** Rush University Medical Center, Chicago, Illinois
**K. Clapp,** FRAXA Research Foundation, Newburyport, Massachusetts

## BACKGROUND

This meeting was the seventh in a series of annual Banbury Center conferences on fragile X, although fragile X was discussed at Banbury long before then, in the early days of applying recombinant DNA techniques to mapping and cloning genes involved in inherited disorders. This meeting took a broad perspective on fragile X, reviewing what is known of *FMR1*/RNA interactions, FMRP cellular biology and the proteins that interact with it, synaptic physiology, and how fragile X affects the nervous system in animal models and humans. A final session discussed progress in the all-important task of developing treatments.

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

**SESSION 1:** Basic Mechanisms of the *FMR1* Gene/RNA Interactions/Cargo RNAs
**Chairperson: B.A. Oostra,** Erasmus Universiteit Rotterdam, The Netherlands

J.R. Fallon, Brown University, Providence, Rhode Island: Axonal FMRP in the developing vertebrate brain.

J. Darnell, The Rockefeller University, New York: G-quadruplex and kissing complex RNA ligands of the fragile-X family of RNA-binding proteins.

S. Ceman, University of Illinois, Urbana: Identification and characterization of the methyl arginines in the fragile-X mental retardation protein.

B. Bardoni, Faculte de Medecine, Nice, France: FMRP and RNA: Old and novel friends.

Y. Feng, Emory University, Atlanta, Georgia: Translation regulation by FMRP during neuronal development.

**SESSION 2:** FMRP Interacting Proteins and FMRP Cellular Biology Including Transport, Signal Transduction, and Mechanisms of Translational Regulation
**Chairperson: S.T. Warren,** Emory University School of Medicine, Atlanta, Georgia

G.J. Bassell, Emory University, Atlanta, Georgia: The stimulating travels and function of FMRP.
P.W. Vanderklish, Scripps Research Institute, La Jolla, California: Novel physiological and proteomic characterization of the *Fmr1* KO mouse.
M. Hayashi, Massachusetts Institute of Technology, Cambridge: A physical and functional interaction between p21-activated kinase and the fragile-X mental retardation protein.
M.V. Catania, Institute of Neurological Sciences, Catania, Italy: mGlu5 receptor expression and interaction with Homer proteins in a mouse model of FRAXA syndrome.
I.J. Weiler, University of Illinois, Urbana-Champaign. FMRP: Some aspects of translational control.
H. Cline, Cold Spring Harbor Laboratory: Control of experience-dependent structural plasticity by local protein synthesis.
E. Klann, Baylor College of Medicine, Houston, Texas: Translational and proteasomal regulation of FMRP during hippocampal mGluR-LTD.

**SESSION 3:** Synaptic Physiology and Function of FMRP Including Effects on LTP/LTD, Glutamate, and GABA Activity
**Chairperson: W.T. Greenough,** University of Illinois, Urbana

O. Steward, University of California, Irvine: Translation of mRNA at synapses in *Fmr1* knockout mice.
K.M. Huber, University of Texas Southwestern Medical Center, Dallas: Role for FMRP in synaptic function and plasticity.
M.F. Bear, Massachusetts Institute of Technology, Cambridge: Tests of the mGluR theory.
S. Chattarji, National Centre for Biological Sciences, Bangalore, India: mGluR- and NMDAR-dependent synaptic plasticity: A contrasting view from the amygdala.
B.A. Oostra, Erasmus Universiteit Rotterdam, The Netherlands: Cerebellar function and the FMR1 knockout mouse
C.L. Cox, University of Illinois, Urbana: Altered synaptic plasticity in sensory neocortex associated with FMRP knockout.
J.R. Larson, University of Illinois, Chicago: Age-dependent impairment of LTP in olfactory cortex of mice lacking FMRP.

**SESSION 4:** Brain Phenotypes Mediated by FMRP Including Dendritic Morphology, Neural Networks/Seizure Generation, Learning, and Behavioral Measures in FXS Models
**Chairperson: J. Darnell,** The Rockefeller University, New York

W.T. Greenough, University of Illinois, Urbana: Spine/synapse phenotype: Context-dependent expression.
I. Bureau, Cold Spring Harbor Laboratory: Defects of functional and anatomical connectivity in the barrel cortex of *fmr1* KO mice.
R.K.S. Wong, SUNY–Health Science Center, Brooklyn, New York: Cellular mechanisms of mGluR-induced epileptogenesis.
M. Zhuo, University of Toronto, Ontario, Canada: Synaptic and behavioral studies of prefrontal cortical potentiation in a mouse model for fragile X.
R.E. Paylor, Baylor College of Medicine, Houston, Texas: Behavior of *Fmr1* KO mice: Genetic interactions.
C.B. Smith, National Institute of Mental Health/NIH, Bethesda, Maryland: In vivo studies of regional brain metabolism in the fragile-X mouse.
D.L. Nelson, Baylor College of Medicine, Houston, Texas: Circadian derangement in *Fmr1/Fxr2* knockout mice: A role for FMR1 in clock control?

**SESSION 5:** A Look at Progress in Moving toward the Goal of Treatment in Humans
**Chairperson: M.R. Tranfaglia,** FRAXA Research Foundation, Newburyport, Massachusetts

S.T. Warren, Emory University School of Medicine, Atlanta, Georgia: A 2000-compound drug screen using *dFmr1*-deficient *Drosophila*.
G. Bilbe, Novartis Institutes for BioMedical Research, Basel, Swtizerland: Exploratory therapeutic approaches to FRX.
F. Gasparini, Novartis Pharma AG, Basel, Switzerland: Identification and characterization of PET-imaging ligands for the mGlu5 receptor.
W. Spooren, Hoffmann-La Roche Ltd., Basel, Switzerland: Fenobam, a clinically validated non-benzodiazepine anxiolytic, is a potent, selective, and noncompetitive mGlu5 receptor antagonist with inverse agonist activity.
E. Berry-Kravis, Rush University Medical Center, Chicago, Illinois: Progress in clinical trial design for FXS treatment trials.
S.C. Landis, National Institute of Neurological Disorders and Stroke/NIH, Bethesda, Maryland: Brief comments about importance of fragile X from NIH's perspective.

# Appetite and Feeding

**April 30–May 3**

FUNDED BY **Cold Spring Harbor Laboratory Corporate Sponsor Program**

ARRANGED BY **J. Friedman,** The Rockefeller University, New York
**S. O'Rahilly,** University of Cambridge, United Kingdom

## BACKGROUND

There is a complex interaction between physiology and psychology in determining when and how much we eat. Biochemical and physiological processes regulate food intake, but this is modified by psychological stimuli relating to the senses of taste, smell, and sight. These studies involve researchers in diverse areas of study and one of the goals of the meeting was to bring together these investigators who may not otherwise meet. The success of the meeting was evident from the range of organisms and topics discussed. These included studies of round worms, fruit flies, snails, and human beings and of smell and taste. One talk was titled "Disgust Discussed"!

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

**SESSION 1:** Studies in Invertebrates
**Chairperson: E.J. Nestler,** University of Texas Southwestern Medical Center, Dallas

C.I. Bargmann, The Rockefeller University, New York: Food quality and the regulation of food preference.
G. Ruvkun, Massachusetts General Hospital, Boston: Functional genomic analysis of *C. elegans* fat control.
L. Vosshall, The Rockefeller University, New York: Genetic control of olfactory perception in *Drosophila.*
R. Gillette, University of Illinois, Urbana-Champaign: Neural circuits integrating appetite, sensation, and experience in foraging decisions.

**SESSION 2:** Feeding in Vertebrates
**Chairperson: G. Barsh,** HHMI/Stanford University School of Medicine, California

M.W. Schwartz, Harborview Medical Center, Seattle, Washington: Integration of homeostatic and satiety signals in food intake regulation.
J.S. Flier, Beth Israel Deaconess Medical Center, Boston, Massachusetts: Hypothalamic neurogenesis and the regulation of energy balance.
J.K. Elmquist, University of Texas Southwestern Medical Center, Dallas: CNS pathways underlying coordinated body weight and glucose homeostasis.
E.J. Nestler, University of Texas Southwestern Medical Center, Dallas: Regulation of brain reward regions by feeding peptides in animal models of addiction and depression.
M.A. Cowley, Oregon Health and Science University, Portland: Cannabinoid antagonists regulate energy balance through the ventral tegmental area, not the melanocortin circuits.

**SESSION 3:** Feeding in Vertebrates
**Chairperson: J.S. Flier,** Beth Israel Deaconess Medical Center, Boston, Massachusetts

R. Cone, Oregon Health Sciences University, Portland, Oregon: Genetics of energy homeostasis in a vertebrate model system.
G. Barsh, HHMI/Stanford University School of Medicine, California: Transcriptional regulation of Agrp expression.
E. Maratos-Flier, Beth Israel Deaconess Medical Center, Boston, Massachusetts: Appetite regulation and drug sensitization: Role of melanin-concentrating hormone in regulating dopaminergic tone.
H. Grill, University of Pennsylvania, Philadelphia: The neural control of feeding and energy expenditure is distributed with nodes in hypothalamus and caudal brainstem.
A.E. Kelley, University of Wisconsin, Madison: Energy, action, and reward: Neural control of food motivation.
B.E. Levin, V.A. Medical Center, East Orange, New Jersey: Metabolic sensing neurons and the control of feeding: The final common pathway to obesity.

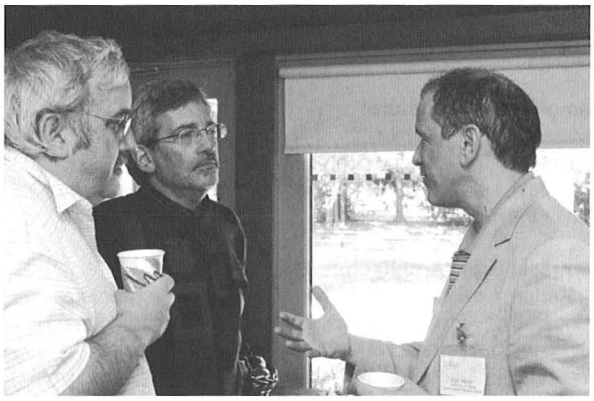
**SESSION 4:** Taste, Smell, and Gut Hormones
**Chairperson: S. O'Rahilly,** University of Cambridge, United Kingdom

U. Boehm, University Hamburg, Germany: Feedback loops link odor and pheromone signaling with reproduction.
M. Zoller, Senomyx, Inc., La Jolla, California: Using human taste receptors to discover novel taste modulators.
S.R. Bloom, Imperial College London, United Kingdom: Mouth, bowel, and brain—Are they connected?
J.M. Friedman, HHMI/The Rockefeller University, New York: Leptin and the neural circuit regulating appetite.

**SESSION 5:** Reward, Addiction, Disgust, and Human Studies
**Chairperson: J.M. Friedman,** HHMI/The Rockefeller University, New York

E. Rolls, University of Oxford, United Kingdom: Neurophysiological and fMRI analyses of the processing of taste and olfactory information in cortical areas related to the control of appetite.
A. Calder, MRC Cognition and Brain Science Unit, Cambridge, United Kingdom: Disgust discussed.
A. Del Parigi, Pfizer Global R&D, Groton, Connecticut: Neuroimaging markers of eating behavior in humans.
S. O'Rahilly, University of Cambridge, United Kingdom: Genetics and human eating behavior.

A. Calder, E. Rolls



S. O'Rahilly, R. Cone, E. Nestler

# Design Principles In Biological Systems

**May 7–10**

FUNDED BY **The Dart Foundation**

ARRANGED BY **P.P. Mitra,** Cold Spring Harbor Laboratory
**J. Doyle,** California Institute of Technology, Pasadena
**R.M. Murray,** California Institute of Technology, Pasadena

## BACKGROUND

Living organisms have been conventionally studied following a reductionist strategy, using the tools of genetics, biochemistry, and cell biology. However, there are also likely to be more general principles involved, and a new theoretical biology is currently taking shape with more formal emphasis on design or engineering principles. For this research program to succeed, biology researchers will need to be trained in the concepts and mathematics relevant to engineering theories, and engineering theorists and physical scientists need training in biological problems. This meeting was a bold start to achieving these goals.

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

**SESSION 1:** Control Theory
**Chairperson: M.E. Csete,** Emory Healthcare, Atlanta, Georgia

R.M. Murray, California Institute of Technology, Pasadena: Tutorial.

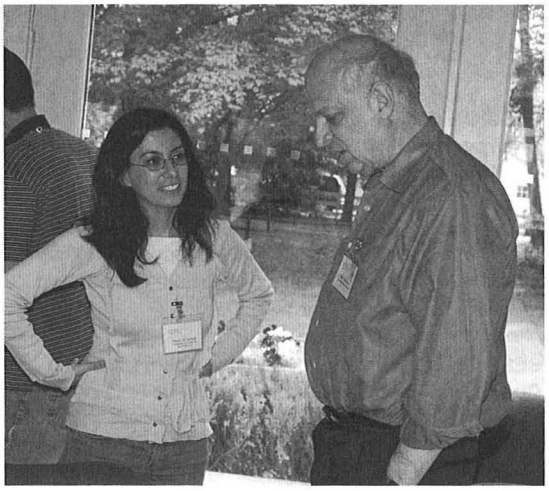
**Examples: Cellular Networks**
M. Khammash, University of California, Santa Barbara: Feedback control and heat shock response in bacteria.
M.A. Savageau, University of California, Davis: Feedback control in cellular metabolism.

**Examples: Insect Locomotion**
M.H. Dickinson, California Institute of Technology, Pasadena: Control mechanisms in insect flight.
P. Holmes, Princeton University, New Jersey: Dynamics and control in insect walking.

**SESSION 2:** Control Theory
**Chairperson: B. Bamieh,** University of California, Santa Barbara

**Examples: Motor Control**
S. Massaquoi, Massachusetts of Technology, Cambridge: Cerebellum as feedback controller.
D. Kleinfeld, University of California, San Diego: Active sensation in the rat vibrissae system.

**Examples: Brain Architecture/Evolution**
H.J. Karten, University of California, San Diego: Architectural principles of vertebrate brains and feedback control.
C.C. Hilgetag, International University Bremen, Germany: Feedback or feedforward? Analysis of visual cortical circuitry.



H. Samad, M. Kirschner

L. Caporale, H. Karten

**SESSION 3:** Control Theory—Human Applications
**Chairperson: J.E. Spiro,** Nature Publishing Group, New York

D. Prelec, Institute for Advanced Study, Princeton, New Jersey: Feedback control and economics.

**Discussion**
**Leader: H. El-Samad,** University of California, San Francisco

**SESSION 4:** Distributed Control and Games
**Chairperson: H. Breiter,** Massachusetts General Hospital and Harvard Medical School, Charlestown

M. Kearns, University of Pennsylvania, Philadelphia: Tutorial: Game theory
B. Bamieh, University of California, Santa Barbara: Tutorial: Distributed control.

**Examples: Evolution of Design**
M.W. Kirschner, Harvard Medical School, Boston, Massachusetts: Facilitated variation.
M. Levine, University of California, Berkeley: Genomic architecture.

**SESSION 5:** Communication Theory
**Chairperson: S.K. Mitter,** Massachusetts Institute of Technology, Cambridge

P. Mitra, Cold Spring Harbor Laboratory: Tutorial.

**Examples: Animal Communication Systems**
P. Narins, University of California, Los Angeles: Time and frequency division multiplexing in frog communication.
T. Fitch, University of St. Andrews, Fife, Scotland: Animal source codes: Vocal adaptations in animals.

**Examples: Linguistic Communications**
P. Niyogi, University of Chicago, Illinois: Human language as a communication system.

**SESSION 6:** Communication Theory—Human Applications
**Chairperson: L.H. Caporale,** Columbia University, New York

J. Doyle, California Institute of Technology, Pasadena: Comparing human technologies and biological systems.

**Discussion**
**Leader: A. Sengupta,** Rutgers, The State University of New Jersey

**SESSION 7:** Computation
**Chairperson: S. Basu,** National Science Foundation, Arlington, Virginia

**Examples: Molecular Circuits**
E. Winfree, California Institute of Technology, Pasadena: Automata and algorithms: Examples from in vitro biochemistry.
B. Mishra, New York University: Tutorial: Theory of computation.
H.S. Seung, Massachusetts Institute of Technology, Cambridge: Examples of automata in neural systems.
C.D. Smolke, California Institute of Technology, Pasadena: Examples from cellular biochemistry.

**Recap and future planning**
**P.P. Mitra,** Cold Spring Harbor Laboratory
**J. Doyle,** California Institute of Technology, Pasadena
**R.M. Murray,** California Institute of Technology, Pasadena

# Parkinson's Disease: Insights from Genetic and Toxin Models

**May 14–17**

FUNDED BY **The Thomas Hartman Foundation for Parkinson's Research**

ARRANGED BY **N. Bonini,** University of Pennsylvania, Philadelphia
**S.E. Przedborski,** Columbia University, New York

## BACKGROUND

Neither the cause nor the mechanism by which neurons degenerate in Parkinson's disease are completely understood. However, scientists now have experimental models developed through gene manipulation and the use of toxins in organisms as varied as primates, rodents, roundworms, and yeast. Cell culture and cell-free systems are also available for investigation of specific aspects of Parkinson's disease. Unfortunately, none of these models replicate all aspects of the disorder and this meeting took up the challenge of deciding how to choose the best model for a given question.

**Introduction:** **S. Gary,** Banbury Center, Cold Spring Harbor Laboratory

**SESSION 1:** Primate Models
**Chairperson: P. Aebischer,** Swiss Federal Institute of Technology, Lausanne, Switzerland

E. Bezard, Universite Victor Segalen-Bordeaux, France: Neuroprotection for Parkinson's disease: Call for clinically driven experimental design in animal models.
J.H. Kordower, Rush University Medical Center, Chicago, Illinois: Use of aged and MPTP-treated monkeys to study PD pathogenesis and experimental therapeutics.
D. Gash, University of Kentucky College of Medicine, Lexington: Toxin-induced and age-associated parkinsonism in rhesus monkeys.

S. Przedborski, M. Beal

**SESSION 2:** Rodent Toxin Model
**Chairperson: R. McKay,** National Institute of Neurological Disorders and Stroke/NIH, Bethesda, Maryland

R.S. Betarbet, Emory University School of Medicine, Atlanta, Georgia: The rotenone model and converging mechanisms in Parkinson's disease.
D.A. Di Monte, The Parkinson's Institute, Sunnyvale, California: Modeling environmental risk factors for Parkinson's disease.
S.E. Przedborski, Columbia University, New York: The MPTP mouse model of PD.
M.F. Beal, Cornell University, New York: Testing novel therapies in the MPTP model of PD.
P.K. Sonsalla, UMDNJ–RWJMS, Piscataway, New Jersey: Acute and chronic administration of MPP+: Models of Parkinson's disease.
M.J. Zigmond, University of Pittsburgh School of Medicine, Pennsylvania: Endogenous mechanisms of neuroprotection in cellular and animal models of Parkinson's disease.

**SESSION 3:** Rodent Models: Genetic
**Chairperson: M.F. Beal,** Cornell University, New York

J. Shen, Harvard Medical School, Boston, Massachusetts: Insights from multidisciplinary analysis of parkin, DJ-1, and PINK1 knockout mice.
X.W. Yang, David Geffen School of Medicine at University of California, Los Angeles: BAC transgenic mouse models of neurodegeneration.
P. Aebischer, Swiss Federal Institute of Technology, Lausanne, Switzerland: Use of viral vectors to create genetic models of Parkinson's disease.
T.C. Sudhof, University of Texas Southwestern Medical Center, Dallas: Toward a functional understanding of synucleins.
R.H. Edwards, University of California, San Francisco: The dynamics of α-synuclein at the nerve terminal.

**SESSION 4:** Invertebrate Models and Stem Cells
**Chairperson: T.C. Sudhof,** University of Texas Southwestern Medical Center, Dallas

N. Bonini, University of Pennsylvania, Philadelphia: Insights from *Drosophila* models for Parkinson's disease.
R. Nass, Vanderbilt University Medical Center, Nashville, Tennessee: Pharmacogenetic analysis in a novel model of Parkinson's disease: Identification of genetic and chemical modulators of dopamine neuron degeneration in *C. elegans*.
P. Muchowski, University of California, San Francisco: Genetic dissection of α-synuclein toxicity using yeast.
R. McKay, National Institute of Neurological Disorders and Stroke/NIH, Bethesda, Maryland: Nigro-striatal disease and the origin of dopamine neurons.
L. Studer, Memorial Sloan-Kettering Cancer Center, New York: Human embryonic stem cells.

**SESSION 5:** Cell and Cell-free Systems
**Chairperson: D. Di Monte,** The Parkinson's Institute, Sunnyvale, California

L.A. Greene, Columbia University, New York: Why neurons die in PD: Insights from a cellular model of the disease.
D. Sulzer, Columbia University, New York: Regulation of cytosolic dopamine in the SN.
P.T. Lansbury, Brigham and Women's Hospital, Cambridge, Massachusetts: Discovering new targets for old drugs: Parkinson's disease therapy in *Drosophila*.
M. Cookson, National Institutes of Health, Bethesda, Maryland: Contribution of kinase activity to the cellular phenotypes of LRRK2 mutants.
A. Maria Cuervo, Albert Einstein College of Medicine, Bronx, New York: Selective autophagy in the pathogenesis of PD.

**Summary**
**S. E. Przedborski,** Columbia University, New York
**N. Bonini,** University of Pennsylvania, Philadelphia
**M.J. Zigmond,** University of Pittsburgh School of Medicine, Pennsylvania

# Spinal Muscular Atrophy: From RNA To Synapses

**September 17–19**

FUNDED BY **Spinal Muscular Atrophy Foundation**

ARRANGED BY **T.M. Jessell,** Columbia University, New York
**C.E. Henderson,** Columbia University, New York
**C. Joyce,** Spinal Muscular Atrophy Foundation, New York

## BACKGROUND

Spinal muscular atrophy is another topic that has been covered in several Banbury Center meetings and it is a further example of how intensive research using the tools of modern experimental biology is leading to a detailed understanding of the molecular and cellular basis of the disorder. Sessions reviewed the latest progress made in analysis of the two survival motor neuron genes and the role of its encoded protein in processing and transport of mRNAs in neurons.

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

**Welcome and Introductions: C.E. Henderson,** Columbia University, New York, and **D. Singh,** Spinal Muscular Atrophy Foundation, New York

**SMA Overview**

D.C. De Vivo, The Neurological Institute, Columbia University Medical Center, New York: SMA clinical features.

K.H. Fischbeck, National Institute of Neurological Disorders and Stroke/NIH, Bethesda, Maryland: SMA research overview.

**SESSION 1:** RNA in Neurons

**Chairpersons: K.C. Martin,** Semel Institute for Neuroscience and Human Behavior, University of California, Los Angeles: Local translation at the synapse during synapse formation and neuronal plasticity; **S.R. Jaffrey,** Weill Medical College, Cornell University, New York: Intra-axonal mRNA translation and neuronal survival.

G.J. Bassell, Emory University, Atlanta, Georgia: Interactions of the SMN complex with localized mRNPs in neuronal processes and growth cones.

G. Dreyfuss, HHMI/University of Pennsylvania School of Medicine, Philadelphia: The SMN complex: Molecular functions and screening for small molecules that affect its expression.

C.E. Beattie, The Ohio State University, Columbus: A zebra fish model of the human motoneuron disease.

A. Krainer, Cold Spring Harbor Laboratory: Strategies for increasing inclusion of SMN2 exon 7.

**Discussants: A. MacKenzie,** Children's Hospital of Eastern Ontario, Canada; **C.E. Beattie,** The Ohio State University, Columbus; **U.R. Monani,** Columbia University Medical Center, New York

**SESSION 2:** The Axon and Synapse

**Chairpersons: B.A. Barres,** Stanford University School of Medicine, California: How are CNS synapses eliminated?; **M.E. Greenberg,** Children's Hospital, Boston, Massachusetts: Signaling networks that regulate synaptic development and cognitive function.

G.S. Battaglia, Neurological Institute, Milano, Italy: The axonal localization of SMN and the role of a-SMN in stimulating axon growth.

Z. He, Children's Hospital Boston, Massachusetts: Axon degeneration and regeneration in SMA.

W. Thompson, University of Texas, Austin: A preliminary examination of the physiology and innervation of hindlimb muscles in the mouse model of type II SMA.

C.C.J. Miller, University of London, United Kingdom: Axonal transport and neurodegeneration.

**Discussants: S. Burden,** Skirball Institute, New York University Medical School; **J. Pierre Julien,** Centre Hospitalier de l'Universite Laval, Quebec, Canada; **T. Gordon,** University of Alberta, Canada

**SESSION 3:** Survival of Neurons; Gene Therapy

**Chairpersons: P. Aebischer,** Swiss Federal Institute of Technology, Lausanne, Switzerland: The issue of delivering therapeutics to motor neurons; **M. Sendtner,** Universitat Wuerzburg, Germany: Characterization of axonal alteration in cell culture and mouse models of SMA.

L.L. Rubin, Curis, Inc., Cambridge, Massachusetts: Small-molecule screens for increased SMN levels in fibroblasts and motor neurons.

S. Artavanis-Tsakonas, Massachusetts General Hospital and Harvard Medical School, Charlestown: Genetic modifier screens for SMN function.

C.T. Sumner, National Institute of Neurological Disorders and Stroke/NIH, Bethesda, Maryland: Histone deacetylase inhibitors for treatment of SMA.

F. Saudou, Institut Curie, Orsay, France: Huntington's disease: Understanding and restoring Huntington function in axonal transport.

**Discussants: B. McCabe,** Columbia University, New York; **D.K. Gifford,** Massachusetts Institute of Technology, Cambridge

**Closing Discussion and Recommendations**

**C.E. Henderson,** Columbia University, New York

**T.M. Jessell,** HHMI/Columbia University, New York

**D. Singh,** Spinal Muscular Atrophy Foundation, New York

# The Biology of Neuroendocrine Tumors

**September 24–26**

FUNDED BY **Verto Institute**

ARRANGED BY **A.J. Levine,** Institute of Advanced Studies, Princeton, New Jersey
**E. Vosburgh,** Verto Institute, Stamford, Connecticut

## BACKGROUND

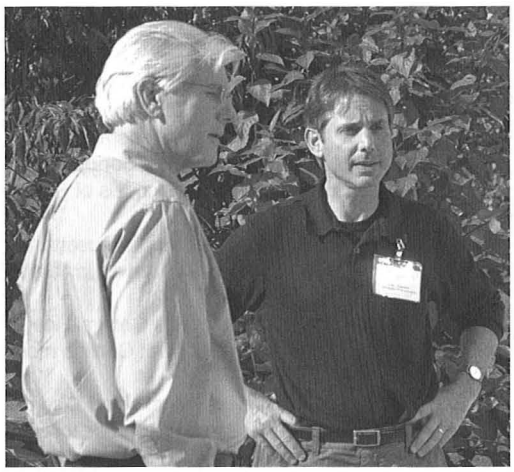
Neuroendocrine tumors are rare tumors with the characteristics of both neural and endocrine cells. Menin was identified as a tumor suppressor involved in multiple endocrine neoplasia type 1 and has been the subject of intensive research. It is a histone methyltransferase, and its role in neuroendocrine cell growth and differentiation and neural crest development was reviewed at this meeting. Data on the characterization of several new cells lines (essential tools for research) were presented, together with genomic analysis of tumor samples. Looking toward therapies, recent progress in clinical trials incorporating receptor tyrosine kinase, mTOR, and VEGF inhibitors was reviewed.

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

## SESSION 1

**Chairperson: A.J. Levine,** Institute of Advanced Studies, Princeton, New Jersey

R.V. Lloyd, Mayo Clinic, Rochester, Minnesota: Characterization of a new carcinoid cell line (HC-45).
G. Van Buren, M.D. Anderson Cancer Center, University of Texas, Houston: The development and characterization of a human midgut carcinoid cell line.
M.L. Meyerson, Dana Farber Cancer Institute, Boston, Massachusetts: Menin function.
X. Hua, University of Pennsylvania, Philadelphia: Menin regulates hematopoiesis and leukemogenesis.
J.A. Epstein, University of Pennsylvania, Philadelphia: Menin has a critical role in neural crest development.
S.K. Kim, Stanford University School of Medicine, California: Calcineurin/NFAT signaling, an essential regulator of neuroendocrine cell growth and function.



E. Vosburgh, J. Epstein

## SESSION 2

**Chairperson: A.J. Levine,** Institute of Advanced Study, Princeton, New Jersey

S. Karnik, Stanford University Medical Center, California: Epigenetic regulation of pathologic and facultative neuroendocrine cell growth.
F. Leu, Verto Institute, Cancer Institute of New Jersey, New Brunswick: Stepping the brake on carcinoid/neuroendocrine tumor by turning on the TGF-β-somatostatin circuitry.
C.J. Barnstable and J. Tombran-Tink, Yale University School of Medicine, New Haven, Connecticut: PEDF inhibits the growth of ovarian and breast cancers.
C. Harris, Verto Institute, Cancer Institute of New Jersey, New Brunswick: CINJ: L1 retrotransposition in neuroendocrine tumors.
D. Klimstra and L. Tang, Memorial Sloan-Kettering Cancer Center, New York: Prognostic classification and gene expression analysis of well-differentiated pancreatic endocrine neoplasms.
M.H. Kulke, Dana Farber Cancer Institute, Boston, Massachusetts: Single-nucleotide polymorphism array analysis of small-bowel carcinoid tumors.
J. Hoh, Yale University School of Medicine, New Haven, Connecticut: Preliminary report on a collaborative carcinoid case control study.

**SESSION 3**
**Chairperson: E. Vosburgh,** Verto Institute, Stamford, Connecticut

M. Essand, Uppsala University, Sweden: A novel chromogranin-a promoter-driven replication-selective oncolytic adenovirus as a therapeutic agent for carcinoid tumors.
K. Oberg, University Hospital, Uppsala, Sweden: 11C-HTP PET in carcinoid and NET.
L. Kvols, University of South Florida, Tampa: Targeted peptide receptor radiotherapy and SOM 230.
J. Yao, Gastrointestinal Medical Oncology, Houston, Texas: Streptizocin-based chemotherapy.
M.H., Kulke, Dana Farber Cancer Institute, Boston, Massachusetts: VEGF TK inhibitors, temazolamide, thalidomide, and lenalinamide therapies.
K. Oberg, University Hospital, Uppsala, Sweden: Biological therapy of NET.
J. Yao, Gastrointestinal Medical Oncology, Houston, Texas: Anti-VEGF and mTOR therapy.
L. Kvols, University of South Florida, Tampa: ENETS-NANETS: What is it and where is it going?

# Chronic Lyme Disease Syndromes: New Avenues for Investigation

**October 15–18**

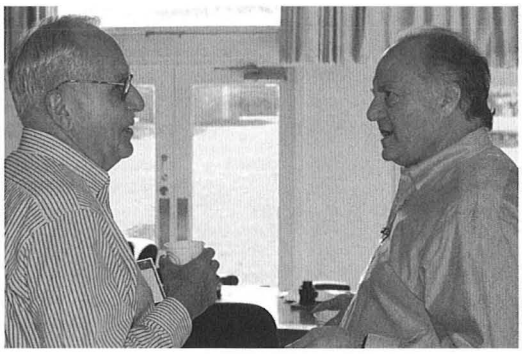
FUNDED BY **Aetos Technologies, Inc., Centers for Disease Control and Prevention (CDC); NIH–National Institute of Allergy and Infectious Diseases, National Institute of Arthritis and Musculoskeletal and Skin Diseases, and National Institute of Neurological Diseases and Stroke; U.S. Food and Drug Administration**

ARRANGED BY **S.E. Schutzer,** UMDNJ–New Jersey Medical School, Newark
**P. Coyle,** SUNY Stony Brook, New York
**J. Dunn,** Brookhaven National Laboratory, Upton, New York

## BACKGROUND

There have been significant advances in the treatment of acute Lyme disease, but many questions remain about those patients who appear to be pathogen-free but continue to exhibit a variety of symptoms. These have been ascribed to many different causes. This is a highly controversial subject and one of great practical importance for individuals who are suffering from these symptoms—How should they be treated? Participants in this meeting discussed three questions: Does the causative agent of Lyme disease, the spirochete *Borrelia burgdorferi,* persist in post-Lyme cases? Might there be other as yet unrecognized coinfections transmitted by the same tick vector? Might spirochete infection trigger long persisting inflammatory symptoms?

**Welcoming Remarks, Goals and Objectives: J.A. Witkowski,** Banbury Center, Cold Spring Harbor Laboratory; **S.E. Schutzer,** UMDNJ–New Jersey Medical School, Newark



P. Baker, S. Schutzer

**SESSION 1:** Can *B. burgdorferi* Persist? Is There an Autoimmune Component in Posttreatment Lyme Cases?

**Chairpersons: P.J. Baker,** National Institute of Allergy and Infectious Diseases/NIH, Bethesda, Maryland; **F.S. Kantor,** Yale University, New Haven, Connecticut

J.L. Benach, SUNY Stony Brook, New York: Discovery of *B. burgdorferi* in ticks. Did we miss other organisms and why?

A.C. Steere, Harvard Medical School, Massachusetts General Hospital, Boston: Discovery of Lyme disease in humans and antibiotic-refractory Lyme arthritis: Persistent infection or autoimmunity.

J.V. Ravetch, The Rockefeller University, New York: Autoimmune approaches in Lyme disease.

S.W. Barthold, University of California, Davis: Persistent infection in animal models and collagen-spirochete interaction and immune evasion.

**SESSION 2:** Postinfectious Responses
**Chairpersons: C.B. Beard,** Centers for Disease Control, Fort Collins, Colorado; **B.J. Luft,** SUNY Stony Brook, New York

S.D. Vernon, Centers for Disease Control and Prevention, CDC, Salida, Colorado: What the human genome can tell us once the pathogen's gone: Lessons learned from chronic fatigue syndrome.

E.S. Raveche, UMDNJ–New Jersey Medical School, Newark: In vivo studies of Bb infection in autoimmune-prone B-cell hyperactive NZB mouse strain.

J.L. Benach, SUNY Stony Brook, New York: Joint *Babesia* and *Borrelia* infections in mice.

L.K. Bockenstedt, Yale University School of Medicine, New Haven, Connecticut: Animal models for the study of *B. burgdorferi* persistence: What do we know and what can we learn?

T.H. Rider, Massachusetts Institute of Technology, Lexington: Novel methods of detecting and inactivating pathogens.

R. Salazar, CytoViva, Aetos Technologies, Inc., Auburn, Alabama: In situ identification and visualization spirochetal structures as *B. burgdorferi*.

**SESSION 3:** Genomics Part 1
**Chairperson: E. Fikrig,** Yale University School of Medicine, New Haven, Connecticut

D.J. Ecker, Ibis Biosciences, Isis Pharmaceuticals, Carlsbad, California: Universal biosensing for pathogen discovery.

**SESSION 4:** Insights from Chronic Lyme Disease Therapy Trials
**Chairperson: P. Coyle,** SUNY Stony Brook, New York

M.S. Klempner, Boston University Medical Campus, Massachusetts: Chronic symptoms following treatment of acute Lyme disease.

P. Coyle, SUNY Stony Brook, New York: Stony Brook trial.

B. Fallon, College of Physicians & Surgeons, New York: Placebo ceftriaxone encephalopathy trial.

A.R. Marques, National Institute of Allergy and Infectious Disease/NIH, Bethesda, Maryland: Framing questions from the clinical sphere.

**SESSION 5:** Microbes in the Tick
**Chairperson: J.L. Benach,** SUNY Stony Brook, New York

D. Fish, Yale University, New Haven, Connecticut: Prevalence and interactions among *I. scapularis*-borne pathogens.

K. Clay, Indiana University, Bloomington: Microbial diversity and interactions in ticks.

**SESSION 6:** Genomics Part 2
**Chairperson: E. Fikrig,** Yale University School of Medicine, New Haven, Connecticut

B.J. Luft, SUNY Stony Brook, New York: Immunologic and phylogenic analysis of OspC: Insights into depth of infection.

**SESSION 7:** Potential Nonmicrobial Action of Antibiotics
**Chairperson: C.B. Beard,** Centers for Disease Control, Fort Collins, Colorado

J.N. Adkins, Pacific Northwest National Laboratory, Richland, Washington: AMT tag proteomics: Application to disease pathogenesis and diagnosis.

J.D. Rothstein, Johns Hopkins University School of Medicine, Baltimore, Maryland: Neuroprotective and inflammatory potential of antibiotics in neurological disease.

D.C. Martz, Rocky Mountain Chronic Disease Specialists, Colorado Springs, Colorado: Motor neuron disease that is antibiotic-responsive.

**SESSION 8:** Rephrasing Questions Amenable to Research
**Chairpersons: P. Coyle,** SUNY Stony Brook, New York; **S.E. Schutzer,** UMDNJ–New Jersey Medical School, Newark

**Outline of suggested blueprint for future research.**
**P.J. Baker,** National Institute of Allergy and Infectious Diseases/NIH, Bethesda, Maryland; **M. Nunn,** National Institute of Neurological Disorders and Stroke/NIH, Bethesda, Maryland: Upcoming federal funding opportunities in the field.

# New Horizons in Internet Site Development

**October 22–25**

FUNDED BY **The William and Flora Hewlett Foundation**

ARRANGED BY **D. Micklos and J. Connolly,** Dolan DNA Learning Center, Cold Spring Harbor Laboratory

**BACKGROUND**

The Internet and the Web are revolutionizing the provision and delivery of information of all kinds, and nowhere more dramatically than in education. However, the design and content presentation of education Web sites are almost certainly not optimal for their function. This workshop brought together workers in a variety of fields, including cognitive science, neuroscience, network theory, knowledge management, learning theory, and technology convergence. They discussed, for example, how knowledge of concept maps can be harnessed to develop Web sites that are more intuitive to use and explore.

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

**SESSION 1:** Insights from Neural and Molecular Science
**Chairperson: M. Smith,** William and Flora Hewlett Foundation, Menlo Park, California

**Opening Remarks: D. Micklos,** Dolan DNA Learning Center, Cold Spring Harbor Laboratory: Introducing *G2C Online*.

J. Connolly, Dolan DNA Learning Center, Cold Spring Harbor Laboratory: Bridging genes and behavior.
H.S. Kurtzman, National Institute of Mental Health/NIH, Bethesda, Maryland: Some current trends in cognitive research.
T. Tully, Cold Spring Harbor Laboratory: Flies R Us revisited: The case for molecular cognition.

**SESSION 2:** Cognitive Science and Network Theory
**Chairperson: M. Smith,** William and Flora Hewlett Foundation, Menlo Park, California

R.M. Shiffrin, Indiana University, Bloomington: Levels of analysis in modeling cognition.
M. Buchanan, La Vignerie, Livarot, France: Evolutionary wisdom and anti-intelligent design.
P. McKercher, Knowledge Web, University of California, Santa Clara: The Knowledge Web as a dynamic knowledge repository.
C. Dietlin, WGBH Interactive West, Greenfield, Massachusetts: Building an Internet site for the classroom.

**SESSION 3:** Multimedia Learning and Education
**Chairperson: E.F. Rover,** Dana Foundation, New York

J.R. Jungck, BioQuest Curriculum Consortium, Beloit College, Wisconsin: Creative commons: Connecting collaborators, cooperating communities, crossing chasms, and celebrating complexity.
J. Bobe, DNA Direct, Inc., San Francisco, California: Citizen science and patient communities on the Web.
J. Kruper, Cardean Learning Group, Chicago, Illinois: What the "participation culture" offers (science) education.
K. Borner, Indiana University, Bloomington: Mapping the structure and evolution of science locally and globally.

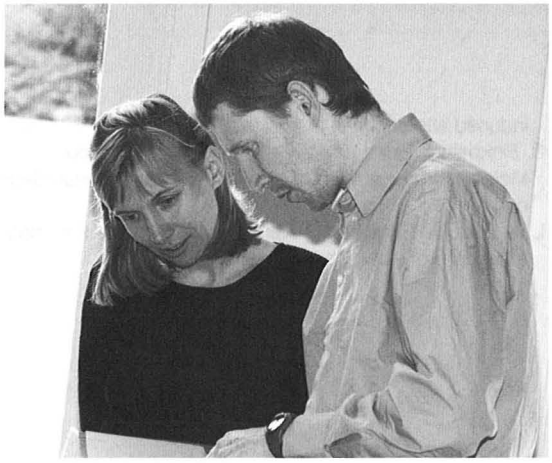
**SESSION 4:** Knowledge Management
**Chairperson: E.F. Rover,** Dana Foundation, New York

J. Novak, Institute for Human and Machine Cognition, University of West Florida, Pensacola: Use of Cmap tools and a new model for education to facilitate learning about genes and cognition.
J. Beisty, SAP Knowledge Management, SAP America, Inc., Newtown Square, Pennsylvania: The business of knowledge management.
S. Buckingham, The Open University, Milton Keynes, United Kingdom: Science portals as hubs for hypermedia discourse.
L. Petrides, Institute for the Study of Knowledge Management in Education, Half Moon Bay, California: Education 2.0: A knowledge management approach.

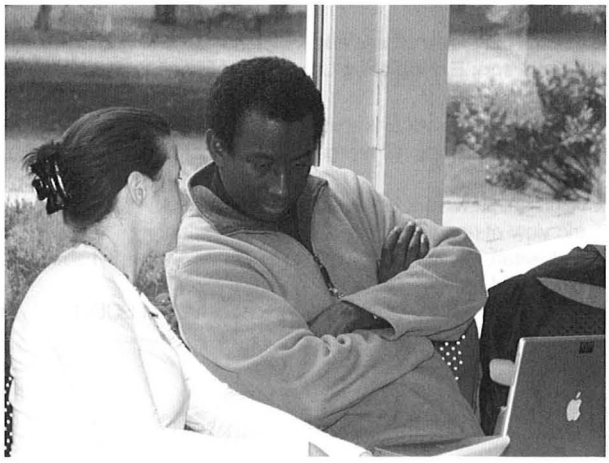
**SESSION 5:** Emerging Technologies
**Chairperson: K. Borner,** Indiana University, Bloomington

W.A. Baer, Annenberg Center for Communication, University of Southern California, Los Angeles: Internet evolution, technological opportunities, institutional constraints.
K. Howell, Federation of American Scientists, Washington, D.C.: Designing games for learning.
H. Heimer, Schizophrenia Research Forum, Providence, Rhode Island: Research forums: Scientist resources and communities online.
L. Stark, University of Utah–Eccles Institute of Human Genetics, Salt Lake City: Exploragraphic: Learning designed for today's tech-savvy students.

**Final Remarks: D. Micklos,** Dolan DNA Learning Center, Cold Spring Harbor Laboratory



K. Borner, J. Connolly



C. Sosnowy, H. Ba

# Axonal Dynamics and Synaptic Junctions

**October 29–31**

FUNDED BY **The ALS Association**

ARRANGED BY **E. Holzbaur,** University of Pennsylvania, Philadelphia
**D.W. Cleveland,** University of California, San Diego
**L. Bruijn,** The ALS Association, Palm Harbor, Florida

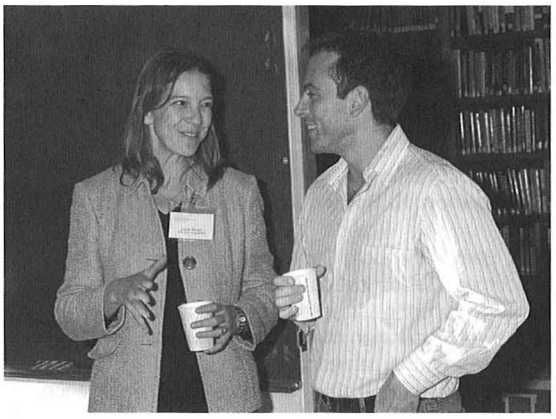
**BACKGROUND**

There is growing interest in the role of axonal dynamics in neurodegenerative diseases including amyotrophic lateral sclerosis (ALS). The recent discovery of dynein/dynactin abnormalities linked to motor neuron degeneration, changes in mitochondrial axonal trafficking in mutant SOD1-expressing mice, and studies showing neuromuscular junction abnormalities in ALS have focused more attention on this area. This workshop reviewed the role of axonal and synaptic junction abnormalities in disease and the potential of therapeutic interventions for ALS targeting these abnormalities.

**Welcome and Introductory Remarks: J.A. Witkowski,** Banbury Center, Cold Spring Harbor Laboratory; **L. Bruijn,** The ALS Association, Palm Harbor, Florida

**SESSION 1:** Axonal Structure and Function
**Chairperson: S. Burden,** New York University Medical School

D.W. Cleveland, University of California, San Diego: Overview of axonal dynamics: Motors, fast and slow axonal transport, and their cargoes.
E. Holzbaur, University of Pennsylvania, Philadelphia: Dynactin/dynein and ALS.
P.J. Hollenbeck, Purdue University, West Lafayette, Indiana: The life of mitochondria in the axon.
G. Banker, Oregon Health and Science University, Portland: Organelle trafficking in hippocampal neurons.
T.L. Schwarz, Children's Hospital, Boston, Massachusetts: Axonal traffic in *Drosophila.*
C.C.J. Miller, University of London, United Kingdom: Axonal transport and neurodegeneration.



L. Bruijn, G. Morfini

**SESSION 2:** Development and Maintenance of Neural Connectivity
**Chairperson: E. Holzbaur,** University of Pennsylvania, Philadelphia

J. Lichtman, Harvard University, Cambridge, Massachusetts: Developmental axonal reorganization: A connectomic approach.
S. Burden, New York University Medical School: A MuSK-centric view of neuromuscular synapse formation.
E.S. Levitan, University of Pittsburgh, Pennsylvania: Synaptic capture of transiting vesicles.
G. Morfini, University of Illinois at Chicago: Mutant SOD-1-induced alterations in fast axonal transport.
S. Finkbeiner, University of California, San Francisco: Molecular mechanisms of Huntington-induced neurodegeneration.
L.W. Enquist, Princeton University, New Jersey: Axon-mediated spread of alpha herpesvirus infections.

**SESSION 3:** Axonal Abnormalities in Neurodegenerative Diseases
**Chairperson: D.W. Cleveland,** University of California, San Diego

W. Mobley, Stanford University, California: Tracking signaling endosomes in axons to decipher neurodegenerative disease mechanisms.

P. Caroni, Friedrich Miescher Institute for Biomedical Research, Basal, Switzerland: Selective vulnerability of fast-fatiguable motoneuron axons.

**SESSION 4:** Model Systems
**Chairperson: L. Bruijn,** The ALS Association, Palm Harbor, Florida

M. Sendtner, Universitat Wuerzburg, Germany: Characterization of axonal alteration in cell culture and mouse models of SMA.

P. Wong, Johns Hopkins University, Baltimore, Maryland: Mechanism of mutant dynactin-induced motor neuron degeneration.

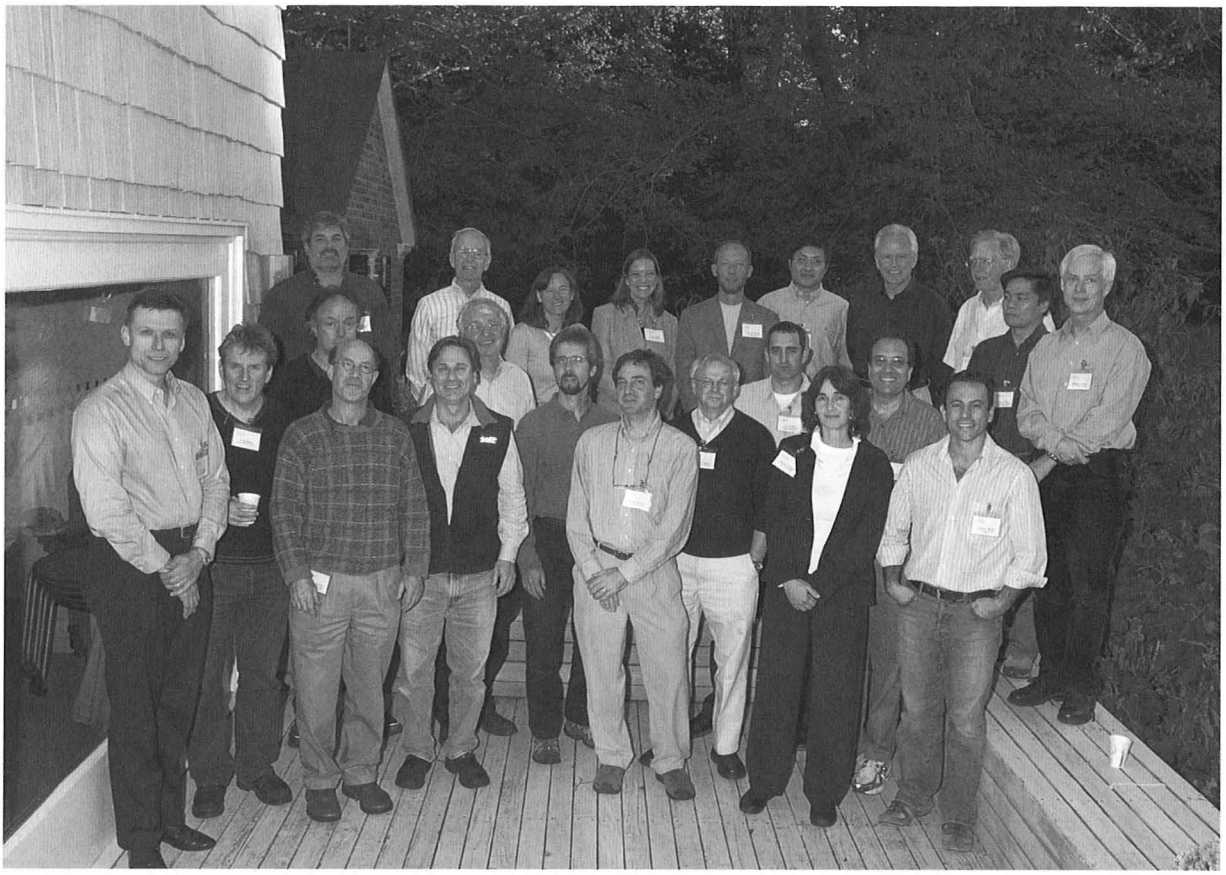
B. Zheng, University of California, San Diego: Axon regeneration in the CNS using mouse models of spinal cord injury.

J.D. Glass, Emory Center for Neurodegenerative Disease, Atlanta, Georgia: Axonal degeneration in neurodegenerative disease: A rational therapeutic target.

M. Coleman, The Babraham Institute, Cambridge, United Kingdom: Common mechanisms of axon degeneration revealed using the slow Wallerian degeneration (*Wlds*) mouse.

E.P. Pioro, The Cleveland Clinic, Ohio: Axonal degeneration and protection of *Wlds* in wobbler motor neuron disease.

L. Reichardt, University of California, San Francisco: Roles of cadherins and caenins at the synapse.



# Integration of Hormonal and Genetic Regulation in Plant Development

**November 5–8**

FUNDED BY **Cold Spring Harbor Laboratory Corporate Sponsor Program**

ARRANGED BY **M. Estelle,** Indiana University, Bloomington
**T. Schmülling,** Free University of Berlin, Institute of Biology/Applied Genetics, Germany
**W. Lukowitz,** Cold Spring Harbor Laboratory

## BACKGROUND

The role of plant hormones in growth development has traditionally been considered separately from the genetic programs that regulate pattern and form. However, with recent advances in our understanding of meristem function, organogenesis, and other developmental processes, it is clear that hormonal and genetic regulations of development are highly integrated. Participants in this meeting discussed questions such as What are the different mechanisms of hormone signaling in plants? How do different hormones act in a synergistic or antagonistic fashion? How do known key genetic players in shoot and root development regulate plant hormones?

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

**SESSION 1:** Pathways and Paradigms
**Chairperson: W. Lukowitz,** Cold Spring Harbor Laboratory

M. Estelle, Indiana University, Bloomington: Function of the TIR1/AFB auxin receptors in plant growth and development.

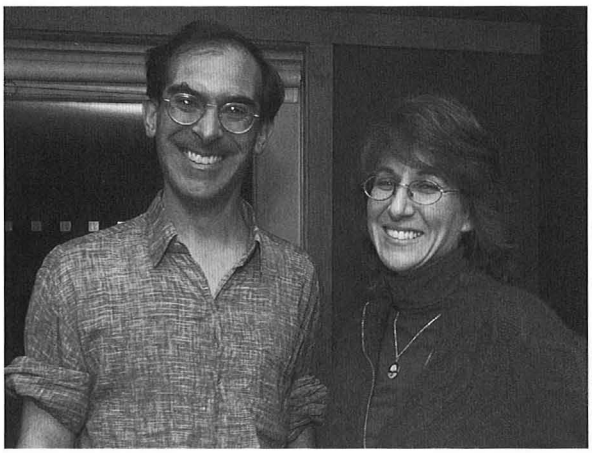
T. Schmülling, Free University of Berlin, Institute of Biology/Applied Genetics, Germany: Cytokinin receptor-mediated developmental pathways.

J. Chory, HHMI/The Salk Institute, La Jolla, California: Using knowledge gained from the Brassinosteroid signal transduction pathway to learn how plants grow.

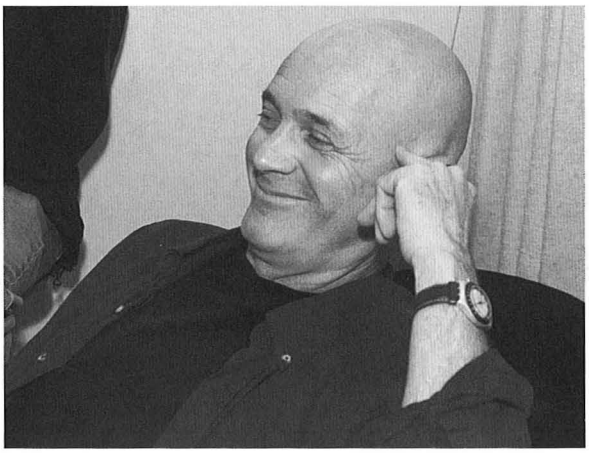
J. Sheen, Massachusetts General Hospital, Boston: MAPK cascades in hormonal signaling.

G. Juergens, Universität Tübingen, Germany: What role for auxin in early embryogenesis?

S. Hake, U.S.D.A. Plant Gene Expression Center, Albany, California: KN1 targets: From maize to *Arabidopsis* and back again.



J. Reed, J. Malamy



D. Weiss

**SESSION 2:** New Players and Cross-talk
**Chairperson: M. Estelle,** Indiana University, Bloomington

J. Friml, ZMBP, Universität Tübingen, Germany: A novel pathway for a nongenomic action of plant hormone auxin.
S. Gilroy, Pennsylvania State University, University Park: C12+ and pH as integrators of plant growth and development.
Z. Yang, University of California, Riverside: ROP GTPases in hormone signaling.
T. Kakimoto, Osaka University, Japan: Paptide mediators that regulate epidermal cell patterning.
W. Lukowitz, Cold Spring Harbor Laboratory: A GATA factor mediating axis and root formation in the early embryo.
J. Long, The Salk Institute for Biological Sciences, La Jolla, California: A role for TOPLESS in embryonic polarity.
P. McCourt, University of Toronto, Canada: Using chemical genetics to map phenotype onto genotype.

**SESSION 3:** Root and Vascular Development
**Chairperson: J. Chory,** HHMI/The Salk Institute for Biological Studies, La Jolla, California

D. Weijers, Wageningen University, The Netherlands: Cell specification and auxin signaling in early embryogenesis.
Y. Helariutta, University of Helsinki, Finland: Integration of hormonal and genetic regulation during plant vascular morphogenesis.
J. Malamy, University of Chicago, Illinois: Hormonal regulation of lateral root formation.
M.J. Bennett, University of Nottingham, Loughborough, United Kingdom: Dissecting the hormonal control of root growth in *Arabidopsis*.
T. Berleth, University of Toronto, Ontario, Canada: Polar signals and gene regulation in vascular development.
J.M. Alonso, North Carolina State University, Raleigh: Ethylene and auxin signaling and response pathways: A paradigm for hormone interaction.

**SESSION 4:** Shoot Development I: Pathway Integration
**Chairperson: T. Schmülling,** Free University of Berlin, Institute of Biology/Applied Genetics, Germany

J. Kieber, University of North Carolina, Chapel Hill: Role of cytokinin signaling in growth and development.
T. Werner, Free University of Berlin, Germany: Cytokinin catabolism regulates the activity of plant meristems.
J. Lohmann, Universität Tübingen, Germany: Regulatory networks of meristem development.
D. Weiss, Hebrew University of Jerusalem, Rehovot, Israel: Role of O-GlcNAc transferase in the interaction between gibberelin and cytokinin response.
J.W. Reed, University of North Carolina, Chapel Hill: Functions of auxin response factors in vegetative and reproductive development.

**SESSION 5:** Shoot Development II: Phyllotaxis and Modeling
**Chairperson: S. Hake,** U.S.D.A. Plant Gene Expression Center, Albany, California

D. Jackson, Cold Spring Harbor Laboratory: Integration of hormonal signals and phyllotaxy.
C. Kuhlemier, University of Bern, Switzerland: Auxin and phyllotaxis.
M. Heisler, California Institute of Technology, Pasadena: Local and global control of auxin transport patterns in the shoot apical meristem.
P. McSteen, Pennsylvania State University, University Park: Genetic and hormonal regulation of axillary meristem initiation during maize inflorescence development.
E. Mjolsness, University of California, Irvine: Integrative mathematical modeling frameworks for plant development.
P. Prusinkiewicz, University of Calgary, Canada: Computational models of auxin-flow-induced patterning in plants.

# Comparative Biology of Innate Immune Systems

**November 27–30**

FUNDED BY **Cold Spring Harbor Corporate Sponsor Program**

ARRANGED BY **J. Dangl,** University of North Carolina, Chapel Hill
**D.A. Portnoy,** University of California, Berkeley
**B.J. Staskawicz,** University of California, Berkeley

## BACKGROUND

Immunity refers to the ability of an organism to resist attack by pathogens. We usually think of immunity as acquired immunity, the response mediated by the vertebrate immune system. However, organisms without immune systems can mount defenses against pathogens through innate immune systems, which, after much neglect, are also the subject of intensive research in human beings. This meeting was notable for bringing together scientists working on innate immunity in plants and animals, to discuss the mechanisms of innate immunity.

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

**SESSION 1:** Plant Intracellular Receptors
**Chairperson: B.J. Staskawicz,** University of California, Berkeley

J. Dangl, University of North Carolina, Chapel Hill: Indirect recognition of pathogen virulence factors by plant NB-LRR disease resistance proteins.

P. Schulze-Lefert, Max-Planck Institute for Plant Breeding Research, Koln, Germany: Molecular links between PAMP- and NB-LRR-triggered immune responses.

J. Ellis, CSIRO, Canberra, Australia: Direct receptor-ligand interaction is the basis of gene-for-gene specificity in the flax-flax rust resistance avirulence gene interaction.

**SESSION 2:** Mammalian Bacterial Pathogenesis
**Chairperson: B.J. Staskawicz,** University of California, Berkeley

D.A. Portnoy, University of California, Berkeley: The mammalian innate immune system: A bacterial perspective.

R.R. Isberg, Tufts University School of Medicine, Boston, Massachusetts: Manipulation of host cell death and survival pathways by *Legionella pneumophila*.

S.I. Miller, University of Washington, Seattle: *Salmonella* interactions with the innate immune system.

**SESSION 3:** Signaling Systems in Plant Innate Immunity
**Chairperson: J. Dangl,** University of North Carolina, Chapel Hill

B.J. Staskawicz, University of California, Berkeley: Host-microbe interactions shaping the evolution of plant innate immunity.
G.B. Martin, Cornell University, Ithaca, New York: Roles of *Pseudomonas* type III effectors AvrPto and AvrPtoB in plant disease susceptibility.
J. Rathjen, John Innes Centre, Colony Norwich, United Kingdom: Specific recognition of AvrPto and AvrPtoB by the Pto/Prf complex in tomato.

**SESSION 4:** TLRs and Host Response
**Chairperson: J. Dangl,** University of North Carolina, Chapel Hill

K. Fitzgerald, University of Massachusetts Medical School, Worcester: Regulation and counter-regulation of type I interferon responses.
L. O'Neill, Trinity College, Dublin, Ireland: Toll-like receptor signal transduction.
D. Golenbock, University of Massachusetts Medical School, Worcester: Anatomy of Toll 9 and its relationship to disease.

**SESSION 5:** Bacterial Type-three Secretion Systems
**Chairperson: D.A. Portnoy,** University of California, Berkeley

J. Galan, Yale University School of Medicine, New Haven, Connecticut: The type III secretion system of *S. enterica*: Decoding its function.
J.E. Dixon, University of California, San Diego School of Medicine, La Jolla: Novel type III pathogenic effectors.
M.B. Mudgett, Stanford University, California: The *Xanthomonas* XopD protease: A generalist or specialist?
U. Bonas, Martin-Luther University, Halle, Germany: Control of *Xanthomonas* type-III secretion and dual activity of the effector AvrBs3 in the plant.
S. Yang He, Michigan State University, East Lansing: Suppression of host innate immune responses by the bacterial pathogen *P. syringae*.
J.T. Greenberg, University of Chicago, Illinois: *P. syringae* type-III effectors: Their functions in host-range determination and the disease process.

**SESSION 6:** Intracellular Receptors II
**Chairperson: J. Galan,** Yale University School of Medicine, New Haven, Connecticut

G. Nunez, University of Michigan Medical School, Ann Arbor: Function of NLRs in innate immunity.
J. Ting, University of North Carolina, Chapel Hill: CATERPILLARs R us: Immune defense genes conserved from plants to mammals.
F.L.W. Takken, University of Amsterdam, The Netherlands: The NB-ARC domain: An NTP-hydrolyzing molecular switch.
R. Innes, Indiana University, Bloomington: Molecular mechanisms underlying the activation of plant NB-LRR proteins.
S. Dinesh-Kumar, Yale University, New Haven, Connecticut: Role of TIR domain in recognition of pathogen-derived elicitors.
J.D.G. Jones, John Innes Centre, Norwich, United Kingdom: Novel approaches to understanding coevolution between plants and filamentous pathogens.

**SESSION 7:** Signaling Systems in Plant and Animal Innate Immunity
**Chairperson: J.D.G. Jones,** John Innes Centre, Norwich, United Kingdom

S. Robatzek, Max-Planck Institute for Plant Breeding Research, Cologne, Germany: Ligand-induced internalization of pattern-recognition receptors in *Arabidopsis* innate immunity.
F.M. Ausubel, Massachusetts General Hospital, Boston: The *C. elegans* innate immune response.
J. Sheen, Massachusetts General Hospital, Boston: Intracellular signaling in plant innate immunity.
R.W. Michelmore, University of California, Davis: Comparative analysis of plant-*Pseudomonas* interactions.
S. Somerville, Carnegie Institution, Stanford, California: The plant cell wall, the first line of defense.
N. Silverman, University of Massachusetts, Worcester: Intracellular recognition of pathogens in *Drosophila.*

J. Jones, J. Ellis, G. Martin

# Redox Regulation of Signal Transduction

**December 3–6**

FUNDED BY **Cold Spring Harbor Laboratory Corporate Sponsor Program**

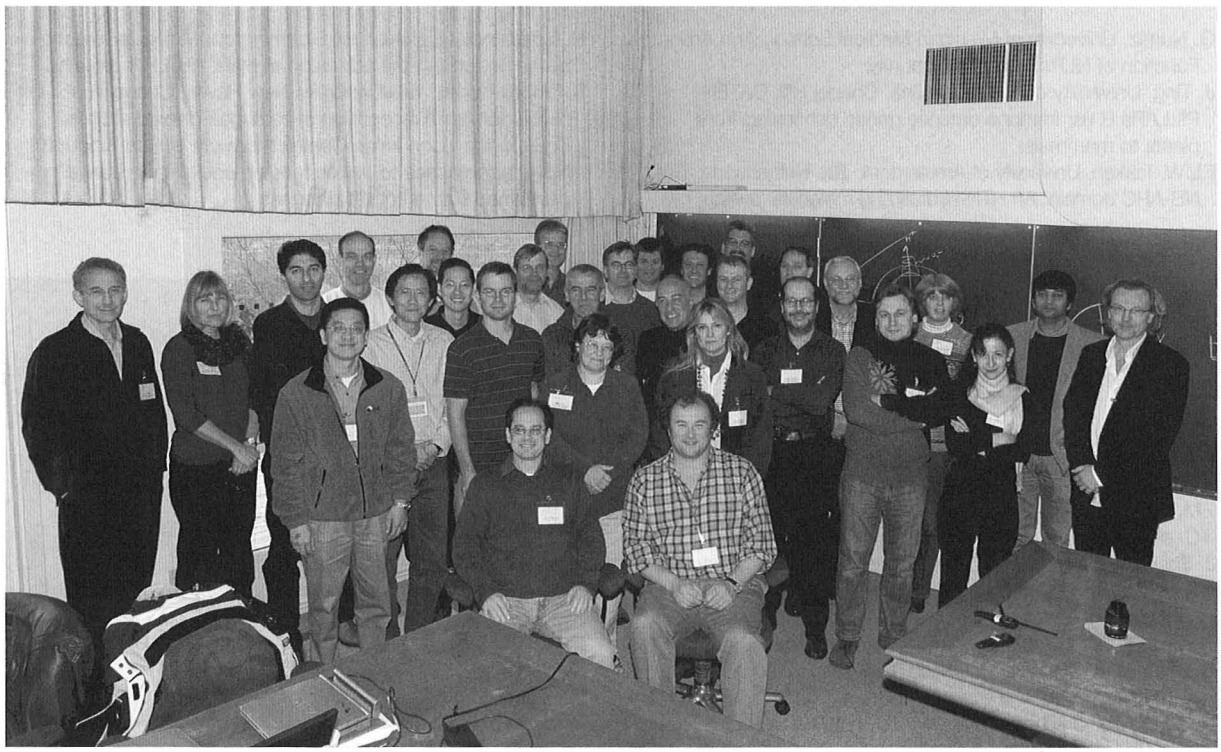
ARRANGED BY **T. Finkel,** National Heart, Lung, and Blood Institute/NIH, Bethesda, Maryland
**S.G. Rhee,** National Heart, Lung, and Blood Institute/NIH, Bethesda, Maryland
**N.K. Tonks,** Cold Spring Harbor Laboratory

## BACKGROUND

Cellular production of reactive oxygen species (ROS) has been associated with a number of disease states as well as the rate of organismal aging. For many years, it was assumed that oxidants functioned within cells in a random and solely destructive manner. In the last decade, evidence has accumulated that ROS can also function within the cell as part of normal signal transduction pathways. This meeting reviewed findings on the specific intracellular targets of oxidants, the range of redox-dependent pathways observed, and the physiological and pathophysiological process specifically regulated by ROS.

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

**SESSION 1:** Sensing ROS Levels
**Chairpersons: T. Finkel,** National Heart, Lung, and Blood Institute/NIH, Bethesda, Maryland; **M. Murphy,** University of Cambridge, United Kingdom



C. Chang, University of California, Berkeley: New chemical approaches to study peroxide biology.
L.B. Poole, Wake Forest University, Winston-Salem, North Carolina: Cysteine sulfonic acids in catalysis and regulation.
V.N. Gladyshev, University of Nebraska, Lincoln: Thiols, selenols, and redox signaling networks.
R. Sitia, Universita Vita-Salute San Raffaele, Milan, Italy: Redox regulation in the endoplasmic reticulum.
J.D. Helmann, Cornell University, Ithaca, New York: Mechanisms of peroxide sensing in bacteria.
M.B. Toledano, LSOC, CEA-Saclay, Gif-sur-Yvette, France: $H_2O_2$ sensing and signaling by thiol-based peroxidases.

**SESSION 2:** ROS Generating/Regulating Systems
**Chairpersons: N.K. Tonks,** Cold Spring Harbor Laboratory; **C.F. Nathan,** Weill Medical College of Cornell University, New York

A. Holmgren, Karolinska Institute, Stockholm, Sweden: Thioredoxin and glutaredoxin systems in redox signaling.
P.T. Schumacker, Northwestern University, Chicago, Illinois: Mitochondrial oxidant generation in response to hypoxia: Compartmental specificity.
M. Murphy, University of Cambridge, United Kingdom: Role of mitochondria in redox signaling.
U.G. Knaus, Scripps Research Institute, La Jolla, California: Regulation and function of epithelial NADPH oxidases.
M.R. Williams, University of Maryland School of Medicine, Baltimore: Expression and function of NADPH oxidases in T lymphocytes.

**SESSION 3:** pTyr Signaling
**Chairperson: L.B. Poole,** Wake Forest University, Winston-Salem, North Carolina

N.K. Tonks, Cold Spring Harbor Laboratory: Regulation of protein tyrosine phosphatase function by reversible oxidation.
A. Ostman, Karolinska Institute, Stockholm Sweden: Regulation of PTPs by hypoxia and ROS.
T.-C. Meng, Institute of Biological Chemistry, Taipei, Taiwan: Redox regulation of protein tyrosine phosphatases by reactive nitrogen species: From molecular identification to signaling implication.
P. Downes, University of Dundee, United Kingdom: Redox regulation of PTEN tumor suppressor amplifies growth-factor-dependent PI3-kinase signaling.
P. Chiarugi, University of Florence, Italy: Hydrogen peroxide: A key messenger for ligand-independent *rtk* activation.
A. Toker, Beth Israel Deaconess Medical Center, Boston, Massachusetts: Protein kinase D signaling in oxidative stress responses.

**SESSION 4:** Signaling and Disease
**Chairpersons**: **P.T. Schumacker,** Northwestern University, Chicago, Illinois; **U.G. Knaus,** Scripps Research Institute, La Jolla, California

G. Gilliland, HHMI/Harvard Medical School, Boston, Massachusetts: FoxO mediates resistance of hematopoietic stems cells to physiologic oxidative stress.
E.V. Avvedimento, University of Naples Federico II, Ancona, Italy: PDGF, ROS, and Ras signals in systemic sclerosis.
K. Griendling, Emory University, Atlanta, Georgia: Regulation of VSMC migratory signals by reactive oxygen species.
J.F. Engelhardt, University of Iowa, Iowa City: Nox-dependent signaling by redox-active endosomes.
C. Taylor, University College Dublin, Ireland: Hypoxia, gene expression, and disease.
C.F. Nathan, Weill Medical College of Cornell University, New York: Reactive oxygen and nitrogen intermediates signal and kill specifically.

**SESSION 5:** Aging and Metabolism
**Chairpersons**: **P. Downes,** University of Dundee, United Kingdom; **K. Griendling,** Emory University, Atlanta, Georgia

T. Finkel, National Heart, Lung, and Blood Institute/NIH, Bethesda, Maryland: Longevity genes as regulators of mitochondrial metabolism.
B.M.T. Burgering, University of Medical Center, Utrecht, The Netherlands: FoxO transcription factor regulation by oxidative stress: Insights into life span and disease.
M. Giorgio, European Institute of Oncology, Milan, Italy: Regulation of adipogenesis by p66Shc-generated oxidative signal.
P. Hwang, National Heart, Lung, and Blood Institute/NIH, Bethesda, Maryland: p53 as a regulator of aerobic respiration.
F. Mechta-Grigoriou, Institute Curie, Paris, France: AP-1, oxidative stress, and aging.

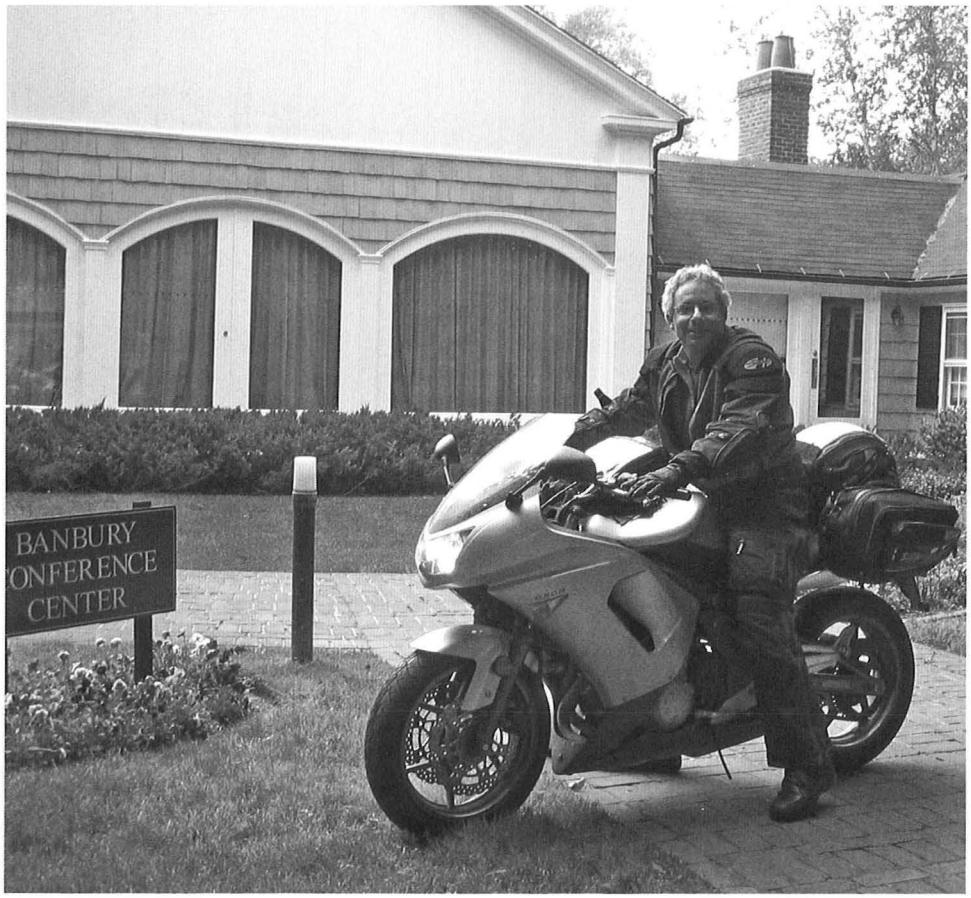
## BANBURY CENTER GRANTS

| *Grantor* | *Program/Principal Investigator* | *Duration of Grant* | *2006 Funding*+ |
|---|---|---|---|
| **FEDERAL SUPPORT** | | | |
| Centers for Disease Control and Prevention (CDC) | Chronic Lyme Disease Syndromes: New Avenues for Investigation | 2006 | $ 7,830* |
| NIH–National Institute of Allergy and Infectious Diseases | Chronic Lyme Disease Syndromes: New Avenues for Investigation | 2006 | 5,000* |
| NIH–National Institute of Arthritis and Musculoskeletal and Skin Diseases | Chronic Lyme Disease Syndromes: New Avenues for Investigation | 2006 | 5,000* |
| NIH–National Institute of Mental Health (through a grant to University of Illinois) | Fragile X Syndrome: Basic Mechanisms and Treatment Implications | 2006 | 47,453* |
| NIH–National Institute of Neurological Disorders and Stroke | Chronic Lyme Disease Syndromes: New Avenues for Investigation | 2006 | 7,000* |
| U.S. Food and Drug Administration | Chronic Lyme Disease Syndromes: New Avenues for Investigation | 2006 | 7,000* |
| **NONFEDERAL SUPPORT** | | | |
| *Meeting Support* | | | |
| Aetos Technologies, Inc. | Chronic Lyme Disease Syndromes: New Avenues for Investigation | 2006 | 10,000* |
| The ALS Association | Axonal Dynamics and Synaptic Junctions | 2006 | 29,311* |
| American College of Medical Genetics | The Evolving Role of the Board-certified Medical Geneticist | 2006 | 10,335* |
| Autism Speaks | A Critical Assessment of Autism Genetics | 2006 | 5,000* |
| Cure Autism Now | A Critical Assessment of Autism Genetics | 2006 | 5,000* |
| The Dart Foundation | Design Principles in Biological Systems | 2006 | 50,000* |
| The Thomas Hartman Foundation for Parkinson's Research | Parkinson's Disease: Insights from Genetics and Toxin Models | 2006 | 25,000 |
| The William and Flora Hewlett Foundation | New Horizons in Internet Site Development | 2006 | 30,200 |
| Nancy Lurie Marks Family Foundation | A Critical Assessment of Autism Genetics | 2006 | 10,000* |
| McLaughlin Centre for Molecular Medicine | A Critical Assessment of Autism Genetics | 2006 | 5,000* |
| National Alliance for Autism Research | A Critical Assessment of Autism Genetics | 2006 | 10,000* |
| Marie Robertson Memorial Fund | The Phenomology of Reconsolidation | 2006 | 20,000 |
| Simons Foundation | A Critical Assessment of Autism Genetics | 2006 | 20,000* |
| Spinal Muscular Atrophy Foundation | Spinal Muscular Atrophy: From RNA to Synapses | 2006 | 42,267* |
| The Stanley Foundation | Research on Genetics of Bipolar Disorder: Current Approaches and Future Directions | 2006 | 7,331* |
| The Swartz Foundation | Computational Approaches to Cortical Function | 2006 | 42,697* |
| Verto Institute | The Biology of Neuroendocrine Tumors | 2006 | 31,490* |
| Volkswagen Foundation | The Phenomology of Reconsolidation | 2006 | 19,572* |

+Includes direct and indirect costs
*New grants awarded in 2006

## Banbury Center Staff

**Jan A. Witkowski,** Executive Director
**Sydney C. Gary,** Assistant Director
**Beatrice Toliver,** Administrative Assistant
**Eleanor Sidorenko,** Secretary
**Barbara Polakowski,** Hostess
**Michael Peluso,** Supervisor, Grounds
**Joseph Ellis,** Groundskeeper




Richard Nass arrives from Vanderbilt University to attend the May 2006 *Parkinson's Disease: Insights from Genetic and Toxin Models* meeting.