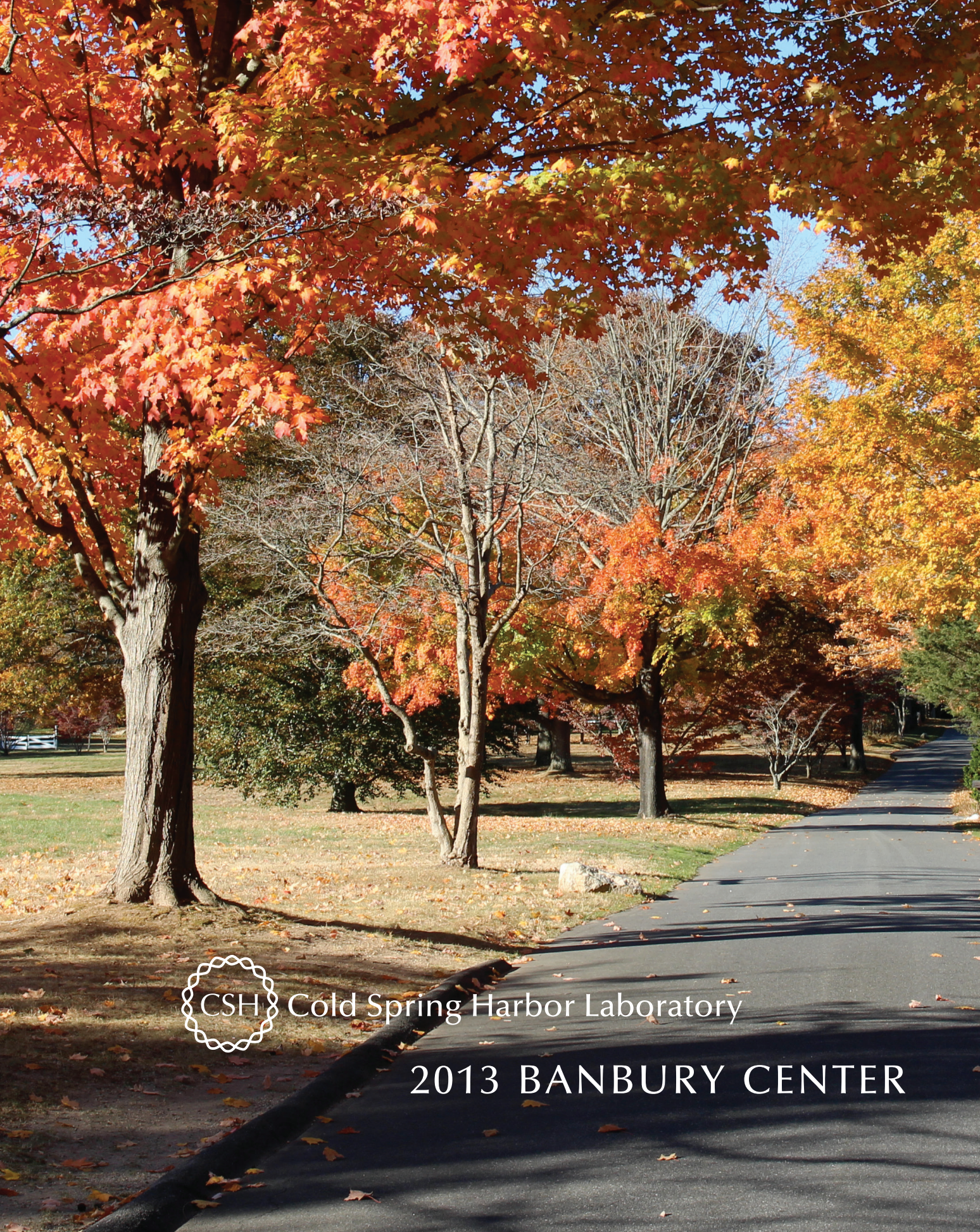
CSH Cold Spring Harbor Laboratory
2013 BANBURY CENTER

BANBURY CENTER

Cold Spring Harbor Laboratory's Banbury Center holds meetings for between 24 and 36 invited participants on topics in biology and biomedical sciences as well as science and healthcare policy. More than 10,000 scientists have participated in the over 600 meetings held since the Center opened in 1978. As of 2013, 69 Nobel laureates have taken part in Banbury Center meetings.

The Center is on a 55-acre estate on the north shore of Long Island, approximately 40 miles east of downtown Manhattan. The estate was donated to the Laboratory in 1976 by Charles Sammis Robertson. The estate's seven-car garage is now the Conference Room, and the family house provides housing for participants. Sammis Hall and Meier House provide additional housing so that everyone attending a Banbury Center meeting can stay on the estate.

Banbury Center meetings are unique among the hundreds of meetings held each year in the United States. The small number of participants ensures that discussions have a major role in each meeting, and the relative isolation of the estate allows participants to focus on the task at hand. Furthermore, because the expenses of participants are covered, selection of scientists is guided by the needs of the science and not dictated by whether those invited can find the funds to attend.

Some of the important Banbury Center meetings include

Patenting of Life Forms. Held just one year after the famous decision in the Diamond vs. Chakrabarty case, patent lawyers and scientists met to discuss the implications of approving patenting of genetically modified bacteria. Nobel laureate Sydney Brenner was a participant.

The Ethos of Scientific Research. Scientific fraud first became a major issue in the late 1980s. This meeting included congressional investigators as well as scientists and ethicists. No fewer than six then or future Nobel laureates attended the meeting.

DNA Technology and Forensic Science. The forensic world began using DNA fingerprinting but without a good understanding of its limitations. The meeting included scientists, prosecutors, defense attorneys, and judges and led to the founding of the Innocence Project by Peter Neufeld and Barry Scheck.

Support for the Center has come from many sources including companies contributing to the Cold Spring Harbor Laboratory Corporate Sponsor Program. Specific meetings have been funded by Pfizer Inc., GlaxoSmithKline, Janssen Pharmaceuticals Inc., Illumina Inc., Sanofi US, and others. The Federal Government has supported meetings through the National Institutes of Health, the National Science Foundation, and the Departments of Energy, Defense, Justice, Agriculture, and Homeland Security. Many foundations have used the Center, including the Amyotrophic Lateral Sclerosis Association, the FRAXA Research Foundation, the Ovarian Cancer Research Fund, and the Swartz Foundation.

Cover: Banbury Lane in Fall

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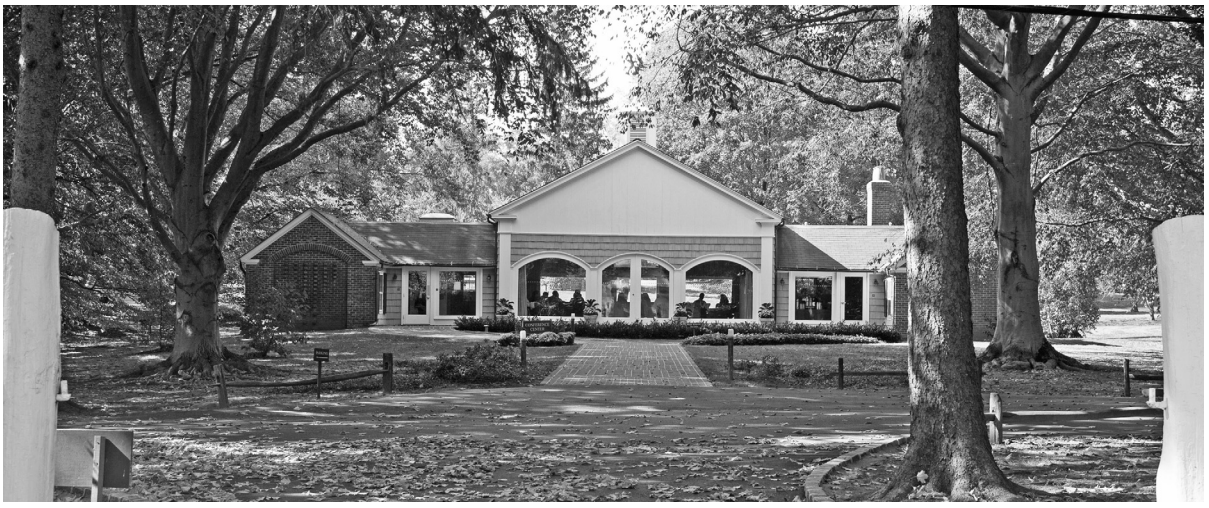
BANBURY CENTER
EXECUTIVE DIRECTOR'S REPORT

It was just over a year ago that our region was devastated by Superstorm Sandy, and I am glad to say that there is little, if any, evidence left of its impact on Banbury. The Robertson House roof was speedily repaired, the debris cleared up, and the fallen trees reduced to chips. The weather continued to be interesting with a major snowstorm in February, 2013, but fortunately Banbury was occupied by the Watson School of Biological Sciences' course on microbial pathogenesis. The participants in the course did not have far to travel to get here.

One lingering effect of the storm was that meetings which were to have been held in 2012 were moved to 2013, so that the year was rather busy. We held 23 meetings with more than 700 participants, in addition to three Watson School courses and six Cold Spring Harbor Laboratory courses. Altogether, the Center was used on 37 occasions in 2013. Participants in the meetings were drawn from no fewer than 40 states, probably a record, although, as usual, four states—California, Maryland, Massachusetts, and New York—accounted for 51% of participants. Twenty-nine percent of participants were female, a proportion that has doubled over the years since 1988, and 50% of the 2013 meetings had at least one female organizer. Banbury meetings continue to have strong international participation with 18% of participants coming from 20 countries.

One of the postponed meetings was on *Redesigning Photosynthesis—Identifying Opportunities and Novel Ideas,* organized by Donald Ort (University of Illinois) and Sabeeha Merchant (University of California, Los Angeles). Nearly all other biological processes on earth depend on the ability of photosynthesis to convert solar energy into chemical energy. There is a great deal of interest in the efficiency with which photosynthesis can accomplish this as it is the basis of the yield potential of both our food and bioenergy crops. In fact, photosynthesis is rather inefficient when all the costs are factored in; in the world's best agricultural regions, ~1% of the total solar energy that falls on the field during the growing season is stored as chemical energy in the plant materials at the end of the season. Participants discussed whether the efficiency of solar energy capture by photosynthesis could be improved even though evolution has provided very little genetic variation in the component mechanisms of photosynthesis.



Conference Room, Fall 2013

The second plant science meeting in 2013 also dealt with metabolism. Organized by Toni Kutchan (Danforth Center, St. Louis), Robert Last (Michigan State University), and Anne Osborn (John Innes Centre, United Kingdom), *Evolution of Plant Metabolic Diversity* focused on the evolution of specialized metabolism in plants. Most classes of specialized compounds are taxonomically restricted, making their analysis less accessible to some of the traditional tools of biology. However, studies of diverse plants, including "nonmodel" species, are benefiting greatly from recent advances in genomics, metabolomics, reverse genetics, and synthetic biology. These tools are allowing rapid enzyme discovery and pathway identification, and the abundance of data across and within taxa creates unprecedented opportunities for comparative analysis. The meeting brought together leaders in studies of these biosynthetic pathways and their functions, along with researchers at the forefront of comparative genomics, evolution, systems, and synthetic biology.

The Banbury Center is known for having meetings on what might be called "emerging topics," and four such meetings took place in 2013. The first was organized by Joshua Dubnau (Cold Spring Harbor Laboratory) and Fred Gage (Salk Institute for Biological Studies). Transposable elements are mobile genetic elements that constitute approximately 50% of the human genome. Some transposable elements have been shown to cause neurodegenerative diseases by insertional mutagenesis, but very recently there have been reports that transposable elements are active during *normal* neurogenesis. This suggests that mobilization of transposable elements in the developing brain might contribute to neuronal diversification. If transposable element mobilization is important in normal brain development, we may need to revise the way we think about the brain.

The involvement of telomeres in aging and aging-related disorders has been known since Carol Greider and Bruce Futcher here at CSHL, together with Calvin Harley at McMaster University, showed that telomeres shorten as human diploid fibroblasts age in cell culture. More recently, a growing body of evidence is implicating telomeres in the pathogenesis of several important degenerative disorders including pulmonary fibrosis, bone marrow failure, and diabetes. However, the underlying role of telomeres in these diverse disorders is not well understood. Is the role of shortened telomere length in these disorders due to effects on stem cells? What is the relationship between telomeres, mitochondria, and cell death? Can measurement of telomere length be a useful diagnostic tool? Will an understanding of the role of telomeres in these disorders point to new therapeutic strategies? Organized by Mary Armanios (Johns Hopkins

Meier House, Winter 2013

Sammis, Winter 2013

University) and Peter Lansdorp (University of Groningen), the meeting brought together scientists and clinicians to review and critically assess current data on how telomere dysfunction contributes to these diseases.

Enhancers—transcriptional regulatory elements that, as their name suggests, enhance gene expression—have been studied for many years. In recent years, there has been rapid progress in identifying transcriptional regulatory elements and the factors that occupy them. In particular, "superenhancers," large clusters of transcriptional enhancers, have been identified. Disease-associated sequence variation occurs in some of these regulatory elements and in the factors that bind them. *Enhancer Biology in Health and Disease*, organized by James Bradner (Dana Farber Cancer Institute), Joanna Wysocka (Stanford University), and Richard Young (Whitehead Institute), brought together experts in enhancer biology to discuss the roles of superenhancers in controlling gene expression and their impact on human health and disease. Topics included basic biology of enhancers (enhancers and chromatin folding, and enhancer dynamics), reviews of the evidence for enhancer involvement in diseases, and how to perform large-scale functional analysis of enhancers identified by sequencing.

Finally, it was a pleasure to have a former Watson School of Biological Sciences student become an organizer of a Banbury Center meeting. Yaniv Erlich left the WSBS with a PhD in 2010 and is now at the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts. Yaniv and his colleagues caused something of a sensation in early 2013, when they published a paper showing that it was possible to recover surnames associated with supposedly anonymized sequence data, using public, freely accessible Internet resources. One concern is whether the ability to do this, even on a limited scale, might lead to restrictions on the availability of genome data. The goals of *Accelerate Genomic Research with Privacy Protections*, organized by Yaniv, Arvind Narayanan (Princeton University), and Robert Kain (Illumina Inc.), were to discuss technical strategies for maintaining privacy of genetic and –omics data sets so that future research would not be compromised. Participants were drawn from an especially wide range of disciplines—human genetics, bioinformatics, cryptography, and ethics.

The continuing success of the Banbury Center program is due to the efforts of many people. Janice Tozzo and Pat Iannotti in the Banbury office, Basia Polakowski at Robertson House, and Jose Pena Corvera, Fredy Vasquez, and Joe McCoy looking after the grounds, all worked

very hard to keep the Center running smoothly. Culinary Services, Facilities, and the Meetings Office played key roles in the operation of the Center. The meetings could not take place without the hard work of the organizers, the generosity of the Laboratory's Corporate Sponsors and the other donors who funded our meetings, and the Laboratory's scientists who continue to support the Center.

Jan Witkowski
Executive Director

Cocktails at the Robertson House

BANBURY CENTER MEETINGS

	Title	*Organizer(s)*
February 3–6	Oxidants and Antioxidants in Cancer Genesis and Treatment	Toren Finkel, Nicholas Tonks, David Tuveson
February 19–22	Interdisciplinary Approaches to Idiopathic Lung Fibrosis	Brigid Hogan, Maria Padilla
February 28–March 3	Grand Challenges in Organismal Biology: Walking the Tightrope between Stability and Change	Dianna Padilla, Billie Swalla, Brian Tsukimura
March 3–6	Evolution of Plant Metabolic Diversity	Toni Kutchan, Robert Last, Anne Osbourn
March 31–April 2	Transposable Elements in the Brain and Other Tissues: Prevalence and Function	Joshua Dubnau, Fred Gage
April 14–16	Development and Evolution of the Human Motor System in Relation to ALS and FTD	Lucie Bruijn, Jeffrey Macklis, Martin Turner
April 19–24	Communicating Science	Sandra Schedler, Claudia Walther
April 28–30	Developing a Neuroscience Consortium	Larry Alphs, Arthur Holden
May 13–16	Redesigning Photosynthesis: Identifying Opportunities and Novel Ideas	Sabeeha Merchant, Donald Ort
July 14–16	The Emerging Intersection between Physical Sciences and Oncology	David Agus, Danny Hillis, Parag Mallick,
September 8–11	Telomeres and Disease	Mary Armanios, Peter Lansdorp
September 15–18	Neurobiology and Clinical Study of Rapid-Acting Antidepressants	Ronald Duman, Carlos Zarate
September 22–25	Plant Reproduction	Robert Martienssen, Robert Meeley
September 29–October 1	Science of Pancreatic Cancer	Ronald Evans, William Isacoff, David Tuveson
October 6–9	Biguanides and Neoplasia	Michael Pollak, Kevin Struhl
October 21–22	Lustgarten Foundation Scientific Meeting	Mila McCurrach
October 23–25	Ovarian Cancer: Developing Research-Based Public Messaging on Early Detection and Screening	Jeffrey Boyd, Audra Moran, Michael Seiden
October 27–30	Enhancer Biology in Health and Disease	James Bradner, Joanna Wysocka, Richard Young
November 12–15	INK4a/ARF Network	David Beach, Norman Sharpless. Charles J. Sherr
December 3–5	The Adolescent Brain	Jay Giedd, Hakon Heimer, Edward Lein, Nenad Sestan
December 8–11	Psychiatric Genomics: Current Status, Future Strategies	W. Richard McCombie, Aarno Palotie
December 11–13	Accelerate Genomic Research with Privacy Protections	Yaniv Erlich, Robert Kain, Arvind Narayanan
December 15–17	Phelan-McDermid Syndrome: Autism Due to Shank3 Mutations/Deletions	Geraldine Bliss, Ricardo Dolmetsch, Craig Powell

BANBURY CENTER MEETINGS

Oxidants and Antioxidants in Cancer Genesis and Treatment

February 3–6

FUNDED BY **John K. Castle**, **Oliver Grace Cancer Fund**

ARRANGED BY **T. Finkel,** National Heart, Lung, and Blood Institute/NIH, Bethesda, Maryland
N. Tonks, Cold Spring Harbor Laboratory
D. Tuveson, Cold Spring Harbor Laboratory

Increased production of reactive oxygen species (ROS) has been functionally linked to aging and cancer. It is now clear that the cellular antioxidant machinery can be up-regulated in response to oncogenes and may confer drug resistance and "stemness." Such observations suggest that redox modulation may offer a new approach for selective targeting of cancer cells. Participants in this meeting explored the chemical, biochemical, and genetic facets of ROS biology in relation to cancer, with the goal of determining whether ROS can be manipulated in vivo to alter cancer pathogenesis and the response of cancer cells to therapy.

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

SESSION 1: Pathways and Redox

Chairperson: T. Finkel, National Heart, Lung, and Blood Institute/NIH, Bethesda, Maryland

T. Finkel, National Heart, Lung, and Blood Institute/NIH, Bethesda, Maryland: Oxidants as signaling molecules.

B. Burgering, University Medical Center Utrecht, The Netherlands: Redox control of FOXO transcription factors to balance life span with disease.

B. Wouters, Ontario Cancer Institute, Toronto, Canada: The role of unfolded protein response on autophagy and ROS during hypoxia.

SESSION 2: Redox Biology

Chairperson: P. Schumacker, Northwestern University, Chicago, Illinois

P. Huang, MD Anderson Cancer Center, Houston, Texas: ROS stress in cancer: Mechanisms and therapeutic implications.

M. Espey, National Cancer Institute/NIH, Bethesda, Maryland: Interplay between mechanobiology, NO, and O_2 in tumors.

SESSION 3: ROS Biology and Chemistry

Chairperson: M. Murphy, University of Cambridge, United Kingdom

M. Murphy, MRC Mitochondrial Biology Unit, Cambridge, United Kingdom: Exploring mitochondrial ROS with targeted molecules.

P. Schumacker, Northwestern University, Chicago, Illinois: Mitochondrial oxidant signals trigger stress responses

N. Chandel, Northwestern University, Chicago, Illinois: Mitochondria regulate cancer.

SESSION 4: ROS Methods and Therapeutic Development

Chairperson: J. Held, Buck Institute for Age Research, Novato, California

J. Held, Buck Institute for Age Research, Novato, California: Mass spectrometric approaches to characterize oxidized cysteines.

T. Dick, German Cancer Research Center, Heidelberg, Germany: In vivo ROS imaging: Concepts, limitations, future directions.

M. Adorno, Institute for Stem Cell Biology & Regenerative Medicine, Stanford University, California: Trisomy of Usp16 contributes to senescence and stem cell defects in somatic tissues of Down syndrome and is associated with breast cancer protection.

Summary Discussion, T. Finkel, National Heart, Lung, and Blood Institute/NIH, Bethesda, Maryland

SESSION 5: Exogenous and Endogenous Antioxidants and Cancer

Chairperson: A. Holmgren, Karolinska Institute, Stockholm, Sweden

A. Holmgren, Karolinska Institute, Stockholm, Sweden: Thioredoxin and glutaredoxin systems in DNA synthesis and control of cell death.

T. Mak, Princess Margaret Hospital, Toronto, Canada: Regulation of oxidants and antioxidants in oncogenic metabolic adaption.

G. Buettner, University of Iowa, Iowa City: Applying quantitative redox biology to understand mechanisms of pharmacological ascorbate in cancer treatment.

SESSION 6: NRF2 and ROS Regulation

Chairperson: J. Hayes, Ninewells Hospital and Medical School, Dundee, United Kingdom

J. Hayes, Ninewells Hospital and Medical School, Dundee, United Kingdom: Roles of transcription factor Nrf2 in adaptation to oxidative stress and tumor growth.

S. Biswal, Johns Hopkins School of Public Health, Baltimore, Maryland: Nrf2 at the crossroad of redox and energy metabolism and therapeutic resistance.

M. Sporn, Dartmouth Medical School, Hanover, New Hampshire: Nrf2: Good or bad for cancer?

SESSION 7: ROS Signaling

Chairperson: S.G. Rhee, Ewha Womans University, Seoul, Korea

S.G. Rhee, Ewha Womans University, Seoul, Korea: Centrosomal accumulation of H_2O_2 through Peroxiredoxin I inactivation is required for mitotic entry.

A. Ostman, Karolinska Institute, Stockholm, Sweden: ROS-mediated regulation of cell signaling through oxidation of tyrosine phosphatases.

S. Muthuswamy, Ontario Cancer Institute, University of Toronto, Canada: Cell polarity, protein scribble, and ROS.

SESSION 8: ROS and p53

Chairperson: K. Vousden, Beatson Institute, Glasgow, United Kingdom

K. Vousden, Beatson Institute, Glasgow, United Kingdom: The role of p53 in regulation of ROS.

R. Sordella, Cold Spring Harbor Laboratory: p53 mutation or splice forms cause mitochondrial ROS.

Summary Discussion: A. Holmgren, Karolinska Institute, Stockholm, Sweden

SESSION 9: ROS and Therapies I

Chairperson: A. Letai, Dana-Farber Cancer Institute, Boston, Massachusetts

I. Blair, University of Pennsylvania, Philadelphia: Serum biomarkers of oxidative stress.

A. Letai, Dana-Farber Cancer Institute, Boston, Massachusetts: Mitochondrial fitness and response to anticancer therapy.

R. Sordella, J. Schlessinger

K. Vousden

G. Wondrak, University of Arizona, Tucson: Teaching old dogs new tricks: Drug repurposing for redox-directed cancer chemotherapy.

D. Spitz, University of Iowa, Iowa City: Metabolic oxidative stress in cancer biology and therapy.

SESSION 10: ROS and Therapies II

Chairperson: B. Stockwell, Columbia University, New York

B. Stockwell, Columbia University, New York: Ferroptosis: An iron-dependent, oxidative form of nonapoptotic cell death.

Final Meeting Summary: D. Tuveson and N. Tonks, Cold Spring Harbor Laboratory

D. Tuveson, N. Chandel

Interdisciplinary Approaches to Idiopathic Lung Fibrosis

February 19–22

FUNDED BY **Elizabeth Livingston Estate**

ARRANGED BY **B. Hogan,** Duke University Medical Center, Durham, North Carolina
M. Padilla, Mount Sinai School of Medicine, New York

M. Padilla, B. Hogan

Idiopathic pulmonary fibrosis (IPF) is a devastating clinical condition for which there is no effective therapy. This meeting brought together an eclectic mix of clinical and basic scientists with the goal of stimulating ideas about the origin and progression of fibrotic lesions in IPF and how new research tools and experimental paradigms can be developed to test them and to move basic studies into the clinic. Sessions followed the traditional Banbury format of short talks and discussion and focused extended discussions. Topics covered included clinical progression and heterogeneity of IPF; genetic and genomic approaches; development of the peripheral lung, including lineage tracing and new mouse models; stem cells and their regeneration in relation to fibrosis; new discoveries related to fibrosis in different organ systems; role of oxidative and ER stress and senescence; the molecular biology of myofibroblasts, pericytes, and other mesenchymal cells; complexities of the extracellular matrix and signaling pathways; the role of immune cells; and progress of clinical trials.

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

Introduction: B. Hogan, Duke University Medical Center, Durham, North Carolina

SESSION 1: Overviews of Clinical Impact, Pathology, and Classification of Idiopathic Pulmonary Fibrosis

M. Padilla, Mount Sinai School of Medicine, New York: Overview of idiopathic pulmonary fibrosis and other fibrosing interstitial pneumonias: Clinical challenges.

K. Leslie, Mayo Clinic, Scottsdale, Arizona: The pathology of idiopathic pulmonary fibrosis, what have we learned in 50 years?

P. Noble, Duke University School of Medicine, Durham, North Carolina: Overview of pathologic heterogeneity in idiopathic pulmonary fibrosis.

Issues to Consider for Meeting

SESSION 2: Genetics and Genomic Approaches to Lung Fibrosis

C. K. Garcia, University of Texas Southwestern Medical Center, Dallas: Genetic heterogeneity of idiopathic pulmonary fibrosis.

S. Guttentag, University of Pennsylvania, Philadelphia: Pulmonary fibrosis in Hermansky Pudlak syndrome

N. Kaminski, University of Pittsburgh Medical Center, Pennsylvania: Novel biomarkers for idiopathic pulmonary fibrosis.

General Discussion

SESSION 3: Cellular Stress, Senescence, and Epithelia-Mesenchymal Interactions in Relation to Fibrosis

M. Armanios, Johns Hopkins University, Baltimore, Maryland: Telomerase and idiopathic pulmonary fibrosis.

S. Savage, National Cancer Institute, Bethesda, Maryland: Dyskeratosis congenita as a model for understanding pulmonary fibrosis.

S. Friedman, Mount Sinai Hospital, New York: Autophagy drives fibrogenic cell activation in tissue injury?

SESSION 4: Fibrosis in Multiple Organ Systems

J. Duffield, University of Washington, Seattle: Kidney, pericytes, and lung fibrosis.

L. Sakai, Shriners Hospital for Children, Portland, Oregon: Fibrosis due to mutations in fibrillin-1.

SESSION 5: Embryonic Development of the Alveolar Regions of the Lung, Lung Stem Cells, and Alveolar Cell Interactions

E. Morrisey, University of Pennsylvania, Philadelphia: Contribution of Wnt2+ mesoderm progenitors to the developing and adult lung.

B. Hogan, Duke University Medical Center, Durham, North Carolina: Alveolar stem cells and fibrosis in the mouse lung.

B. Hinz, University of Toronto, Canada: Myofibroblast mechanics.

R. Chambers, Centre for Respiratory Research, Rayne Institute, London, England: Coagulation cascade and pulmonary fibrosis.

SESSION 6: Proliferation and Differentiation of Myofibroblasts and Other Mesenchymal Cells (Pericytes, Vascular Smooth Muscle, Lipofibroblasts, Fibrocytes) and Matrix

P. Noble, Duke University School of Medicine, Durham, North Carolina: Regulation of severe pulmonary fibrosis: Roles of the ECM.

L. Olson, Oklahoma Medical Research Foundation, Oklahoma City: PDGF signaling and fibrosis.

K. Leslie, P. Ward, B. Stillman

SESSION 7: Immune System and Lymphatics

I. Rosas, Brigham and Women's Hospital, Boston, Massachusetts: NLRP3 inflammasome activation and experimental pulmonary fibrosis.

C. Becker, Mount Sinai School of Medicine, New York: The role of dendritic cells in idiopathic pulmonary fibrosis.

W. Bradford, InterMune, Inc., Brisbane, California: Idiopathic pulmonary fibrosis clinical trial efficiency.

P.A. Ward, University of Michigan, Ann Arbor: Regulation of the lung inflammatory response by the adrenergic and cholinergic nervous systems.

C. Hogaboam, University of Michigan, Ann Arbor: Innate immune signaling and fibrosis.

D. Wilkes, Indiana University School of Medicine, Indianapolis: Autoimmunity to type V collagen in idiopathic pulmonary fibrosis pathogenesis.

General Discussion

SESSION 8: Clinical Trials

S. Violette, Biogen Idec, Cambridge, Massachusetts: Developing a biomarker strategy to support the early clinical development of STX-100 in IPF patients.

S. Friedman, Mount Sinai Hospital, New York: Defining therapeutic targets for antifibrotic therapies: Challenges and opportunities.

General Discussion and Wrap Up, Potential Areas for Future Collaboration

Impromptu seminar

Grand Challenges in Organismal Biology: Walking the Tightrope between Stability and Change

February 28–March 3

FUNDED BY **Stony Brook University through a grant from the National Science Foundation**

ARRANGED BY **D. Padilla,** Stony Brook University, New York
B. Swalla, University of Washington, Seattle
B. Tsukimura, California State University, Fresno

A central paradox in biology is that animals must maintain the integration of complex developmental and functional systems while simultaneously responding and adapting to continuously changing internal and external environments. Understanding how animals maintain the balance between integrated stability and flexibility (both short-term accommodation and long-term evolutionary adaptation) is of growing importance. However, we do not understand the functional and system-level attributes of animals that make them resilient or robust to internal or external environmental perturbation or, conversely, sensitive or fragile. In particular, we need to understand mechanisms that mediate phenotypic responses to environmental inputs across different scales and to develop quantitative frameworks for analyzing these phenomena. Participants identified critical areas and questions that require new information or approaches, and priorities for new research agendas to address this grand challenge.

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

I. **Introduction of the Grand Challenge of Organismal Biology**
   a. History from NSF to this meeting
      i. GCOB in general
      ii. Selection of walking a tightrope as a first effort
   b. Discussion of Steering Meeting: Goals and challenges
   c. Vision Statement: Transformation of community
   d. Guidelines and deliverables from this big meeting

II. **Question and Answer Session**
III. **What Have Other Communities Done That Are Successful?**
   a. NCEAS example: Building the next generation of scientist
   b. iPlant
IV. **Tutorial: Control Theory (T. Daniel and N. Cowan)**
   a. A control theorist's view on organismal biology (stability): A tutorial
   b. How can control theory be used to answer this GCOB?
   c. How do dynamics interact among scales?
V. **Instructions and Ground Rules for Breakout Sessions**
VI. **First Breakout Session**
   What are the most important, burning questions explicitly across temporal, spatial, and organizational scales related to stability and change?
   What new approaches can/should we use to address these questions?
VII. **Second Breakout Session**
   What are the major challenges or impediments to addressing the burning questions beyond capacity building or just more funding in general?
   Are there specific needs or approaches that would jump-start making progress (e.g., specific national opportunities to facilitate and amplify interactions, targeted research centers)? What they would target, RCNs for mining existing data, and what areas would be most profitable?
   What would your wish list be for solving these questions?
VIII. **Third Breakout Session**
   What are the mutual benefits and deliverables of a new set of approaches for organismal biology, recognizing that the dynamics occurring on all levels of biological organization are inextricably linked?
IX. **Fourth Breakout Session**
   Given steering committee recommendations, what are the short-term and long-term best ways to move forward to answering this GCOB?
   What are the most easily accomplished (low-hanging fruit) and targeted funding priorities?
X. **Grand Synthesis of What We Have Accomplished**
XI. **Next Steps**

D. Plachetzki, D. Grunbaum, Z. Cheviron, J. Marden, M. Hale

Evolution of Plant Metabolic Diversity

March 3–6

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

ARRANGED BY **T. Kutchan,** Danforth Center, St. Louis, Missouri
R. Last, Michigan State University, East Lansing
A. Osbourn, John Innes Centre, Norwich, United Kingdom

This is an exciting time for investigation of specialized (secondary) metabolism in plants. Most of these specialized compounds are taxonomically restricted, making their analysis less accessible to some of the traditional tools of biology. However, studies of diverse plants are benefiting greatly from recent advances in genomics, metabolomics, reverse genetics, and synthetic biology. The abundance of data across and within taxa is creating unprecedented opportunities for comparative analysis. Given the important ecological functions of these molecules, it is not surprising that examples of evolutionary plasticity and strong phenotypic diversity are being uncovered for a variety of biosynthetic pathways. This meeting focused on the evolution of specialized metabolism in plants. Participants included leaders in studies of biosynthetic pathways and researchers at the forefront of comparative genomics, evolution, systems, and synthetic biology.

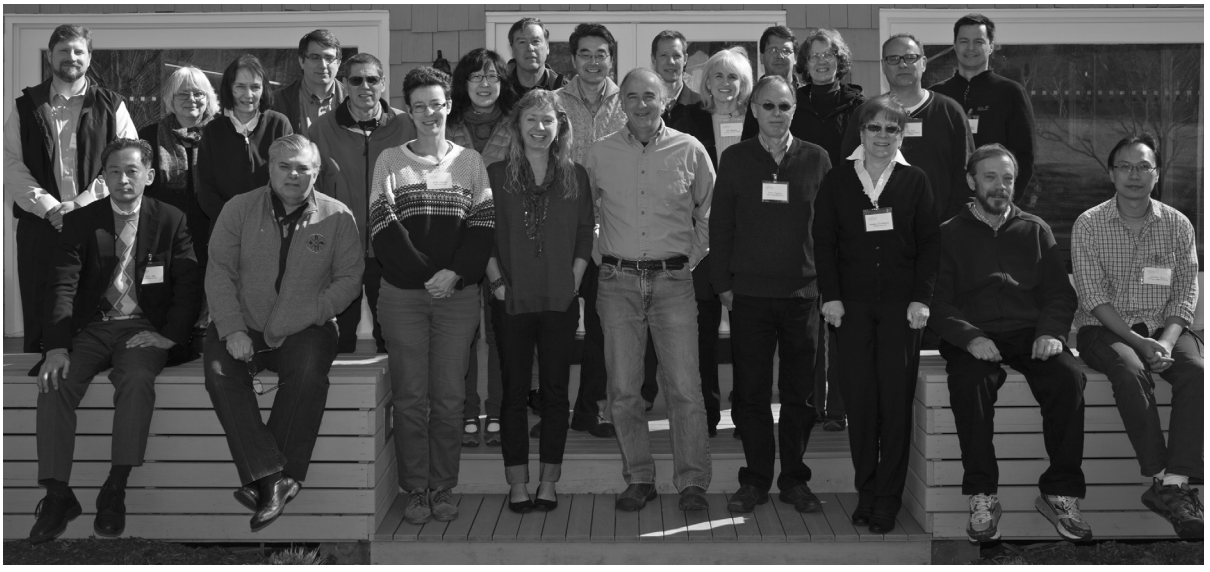
Welcoming Remarks: **J.A. Witkowski,** Banbury Center, Cold Spring Harbor Laboratory

Introductory Remarks: **R. Last,** Michigan State University, East Lansing

SESSION 1: Metabolite Diversity in an Evolutionary/Functional Context

Chairperson: T. Kutchan, Danforth Center, St. Louis, Missouri

R. Last, Michigan State University, East Lansing: Signatures of evolution in glandular trichomes of *Solanum.*



K. Saito, Riken Plant Science Center, Chiba University, Japan: Origin of metabolomic diversity.
M. Simmonds, Royal Botanic Gardens, Kew, London, England: Plant chemosystematics: New opportunities for selecting plants.
E. Kellogg, University of Missouri, St. Louis: Secondary metabolism in the Poaceae (grasses).
T. Mitchell-Olds, Duke University, Durham, North Carolina: Metabolism and complex traits.

General Discussion

SESSION 2: Regulation of Metabolism

Chairperson: A. Osbourn, John Innes Centre, Norwich, United Kingdom

N. Doudareva, Purdue University, West Lafayette, Indiana: An alternate microbial pathway contributes to phenylalanine biosynthesis in plants.
D.J. Kliebenstein, University of California, Davis: Evolution of regulatory links between primary and secondary metabolism.
H. Klee, University of Florida, Gainesville: Regulation of flavor-associated chemical accumulation in the tomato fruit.
M. Lange, Washington State University, Pullman: Evolution of specialized plant tissues and cell types for the synthesis and accumulation of terpenoids.
V. DeLuca, Brock University, Ontario, Canada: Specialized metabolism and the recruitment of multiple cell types for functional pathway organization.

General Discussion

SESSION 3: Pathway Evolution

Chairperson: R. Last, Michigan State University, East Lansing

A. Osbourn, John Innes Centre, Norwich, United Kingdom: Pathway evolution.
E. Pichersky, University of Michigan, Ann Arbor: Terpene gene evolution, evolution of functional gene clusters.
D. Werck-Reichhart, Institute of Plant Molecular Biology, Strasbourg, France: Cytochromes P450 as landmarks of plant metabolism evolution.
E. Wurtzel, City University of New York–Lehman College, Bronx, New York: Enzyme evolution and topological control of carotenoid biosynthesis in plants.
E. Cahoon, University of Nebraska, Lincoln: Evolution of unusual fatty acid synthesis: The case of acetylenic fatty acids and polyacetylenes.

General Discussion

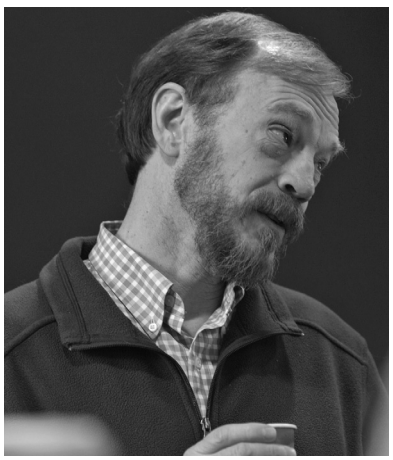
SESSION 4: Omics Approaches to Studies of Pathway and Genome Evolution

Chairperson: H. Klee, University of Florida, Gainesville

S.-H. Shiu, Michigan State University, East Lansing: Metabolic gene duplication and functional divergence/convergence.
S. Rhee, Carnegie Institution of Washington, Stanford, California: Genomic signatures of specialized metabolism evolution in plants.
T. Mockler, Donald Danforth Plant Science Center, St. Louis, Missouri: Informing metabolic studies using transcriptome profiling.
T. Kutchan, Danforth Plant Science Center, St. Louis, Missouri: Using genomics to elucidate biochemical pathways.

General Discussion

SESSION 5: Applying Evolutionary Principles to Pathway Engineering



T. Mitchell-Olds

C. Paddon, E. Wurtzel

Chairperson: K. Saito, Riken Plant Science Center, Chiba University, Japan

I. Abe, University of Tokyo, Japan: Engineered biosynthesis of plant polyphenols.

C. Paddon, Amyris, Inc., Emeryville, California: Semisynthetic Artemisinin: Using synthetic biology to increase the supply of a crucial antimalarial drug.

R. Peters, Iowa State University, Ames: To gibberellins and beyond! The evolution of (Di)terpenoid metabolism.

J. Noel, Salk Institute for Biological Studies, La Jolla, California: The remarkable pliability and promiscuity of specialized metabolism.

Summary Discussion

Conference Room, Winter 2013

Transposable Elements in the Brain and Other Tissues: Prevalence and Function

March 31–April 2

FUNDED BY **Dart NeuroScience and the Marie Robertson Research Fund**

ARRANGED BY **J. Dubnau,** Cold Spring Harbor Laboratory
F. Gage, Salk Institute for Biological Studies, San Diego, California

The functions, if any, of transposable elements (TEs) in the human genome are largely unknown. However, they do cause disease by insertional mutagenesis and have been linked to neurodegenerative diseases. These include transmissible prion disorders, amyotrophic lateral sclerosis, frontotemporal lobar degeneration, macular degeneration, fragile-X-tremor ataxia, and normal aging. There are recent reports that several types of TEs are active during *normal* neurogenesis in mammals and invertebrates. It has been suggested that active mobilization of transposable elements in the developing brain can produce somatic neuronal genetic heterogeneity and that this somatic variation may contribute to neuronal diversification. Participants critically reviewed the state of the field, and the meeting concluded with a session devoted to considering future lines of research, discussing how to promote this area of research, and how to encourage funding by foundations and NIH.

F. Gage, H. Kazazian, A. Ferguson-Smith

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

Introduction: J. Dubnau, Cold Spring Harbor Laboratory

SESSION 1: Transposons and Genome Evolution

Chairperson: R. Martienssen, Cold Spring Harbor Laboratory

R. Martienssen, Cold Spring Harbor Laboratory: Transposons at Cold Spring Harbor Laboratory

P. Batut, Cold Spring Harbor Laboratory: Transposons and evolution of transcriptional regulation in the *Drosophila* clade.

A. Ferguson-Smith, University of Cambridge, United Kingdom: Large clusters of LINE1 repeats: Functional or junk?

K. Kosik, University of California, Santa Barbara: The emergence of brain noncoding RNAs at the Catarrhini Branch.

K. Burns, Johns Hopkins University School of Medicine, Baltimore, Maryland: Mapping and functional analysis of transposable element insertions.

M.C. Marchetto, Salk Institute for Biological Studies, La Jolla, California: Differential LINE-1 retrotransposition in induced pluripotent stem cells between humans and great apes.

SESSION 2: Functional Roles and Regulatory Mechanisms

Chairperson: F. Gage, Salk Institute for Biological Studies, San Diego, California

O. Voinnet, Swiss Federal Institute of Technology Zurich, Switzerland: RNAi-dependent and -independent control of LINE1 mobility and accumulation in mouse ES cells.

K. Creasey, Cold Spring Harbor Laboratory: Plants catch transposons in the act: Control when methylation fails.

S. Waddell, University of Oxford, England: Transposition-driven genomic heterogeneity in the *Drosophila* brain.

C. Walsh, Boston Children's Hospital, Cambridge, Massachusetts: Single-neuron, whole-genome analysis of L1 retrotransposition in the human brain.

A. Muotri, University of California, San Diego, La Jolla: Impact of L1 retrotransposition in the nervous system.

J. Moran, University of Michigan Medical School, Ann Arbor: Studies of a human retrotransposon.

P. Batut photographing Barbara McClintock's corn cobs

SESSION 3: Dysfunction and Disease

Chairperson: S. Martin, University of Colorado, Aurora

J. Dubnau, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York: Jumping into neurodegeneration.

R. Hunter, Rockefeller University, New York: Stress and hippocampal transposable element expression.

P. Jin, Emory University School of Medicine, Atlanta, Georgia: Transposable elements in neurodegeneration.

H. Kazazian, Johns Hopkins University, Institute of Genetic Medicine, Baltimore, Maryland: Extensive somatic L1 retrotransposition in colon cancer.

A. Nath, National Institutes of Health, Bethesda, Maryland: Human endogenous retroviruses in ALS.

Summary, Discussion, and Future Research

Development and Evolution of the Human Motor System in Relation to ALS and FTD

April 14–16

FUNDED BY **Greater New York Chapter of the ALS Association**

ARRANGED BY **L. Bruijn,** ALS Association, Washington, DC
J. Macklis, Harvard University, Cambridge, Massachusetts
M. Turner, University of Oxford, United Kingdom

The neurodegenerative process characteristic of amyotrophic lateral sclerosis (ALS) may be regarded as a system failure on several levels. The mechanisms of spread and of the variable penetrance of pathology within extramotor, upper and lower motor neuronal populations (and supporting cells) remain uncertain, but they are critical to hopes of therapeutic intervention. Data suggest that wider cortical organization, local circuits, and developmental factors may be important in defining vulnerability to neurodegenerative disorders. The neocortical evolutionary changes involved in bipedalism with opposable thumbs, and the relative athleticism observed premorbidly among patients, have been postulated to hold particular relevance for ALS. An understanding of the development and evolution of the motor system and its frontotemporal connections has the potential to re-frame thinking on the pathogenesis of both ALS and FTD. This symposium was the first to draw together a multidisciplinary group of internationally leading neuroscientists who might not otherwise interact.

Welcoming Remarks: J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory
Introduction: L. Bruijn, ALS Association, Washington, DC

SESSION I

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

M. Turner, University of Oxford, John Radcliffe Hospital, United Kingdom: Introduction: From Charcot to C90rf72.

K. Talbot, University of Oxford, John Radcliffe Hospital, United Kingdom: The clinical spectrum of disorders affecting the motor neuron.

V.R. Edgerton, University of California, Los Angeles: Evolutionary organization of motor control circuitry.

A. Eisen, University of British Columbia, Canada: Evolutionary considerations in the pathogenesis of ALS: A clinical perspective.

SESSION II

Chairperson: J. Rothstein, Johns Hopkins University School of Medicine, Baltimore, Maryland

J. Martin, City College of New York, New York: Circuit function: Corticospinal and descending systems.

J. Macklis, Harvard University, Cambridge, Massachusetts: Molecular logic of corticospinal motor neuron development and broader neuron class evolution.

W. Seeley, University of California, San Francisco: Selective neuronal and network-based vulnerability in frontotemporal dementia.

SESSION III

Chairperson: J. Ravits, University of California, San Diego

Z. Molnár, University of Oxford, United Kingdom: The earliest cortical circuits.

S. Pfaff, Salk Institute for Biological Studies, La Jolla, California: Spinal motor neuron development.

J. Rothstein, Johns Hopkins University School of Medicine, Baltimore, Maryland: Cell vulnerability and the role of non-neuronal cells and interneurons in MND.

G. Miles, University of St. Andrews, Fife, Scotland, United Kingdom: Physiology and pathology of spinal motor circuitry.

R. Brownstone, Dalhousie University, Halifax, Nova Scotia, Canada: Control of spinomuscular circuits.

M. Hallett, National Institute of Neurological Disorders, Bethesda, Maryland: Spinal cord circuitry and function.

SESSION IV

Chairperson: A. Al Chalabi, Kings College, Institute of Psychiatry, London, England

A. Al Chalabi, Kings College, Institute of Psychiatry, London, England: Introductory remarks to tie the session together.

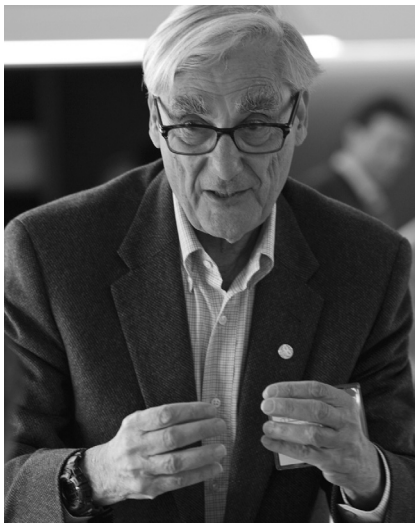
D.W. Dickson, Mayo Clinic, Jacksonville, Florida: The emerging neuropathological taxonomy of ALS and FTD. The range of ALS and FTD phenotypes and their overlap: A pathological view.

M. Strong, Schulich School of Medicine & Dentistry, Ontario, Canada: The emerging neuropsychological spectrum of frontotemporal dysfunction in ALS.

SESSION V

Chairperson: M. Benatar, University of Miami Hospital, Miller School of Medicine, Florida

J. Ravits, University of California, San Diego: Clinicopathological observations on spread in ALS.



A. Eisen

S. Pfaff, J. Rothstein

J. Shefner, State University of New York, Upstate Medical University, Syracuse: Lower motor neuron studies evaluating spread of disease burden.

G. Fishell, New York University Medical Center, New York: Interneuron development.

E. Azim, Columbia University, New York: Genetic manipulation of circuits for skilled forelimb movement in mice.

M. Kiernan, Institute of Neurological Sciences, Neuroscience Research of Australia, Sydney: Cortical excitability in ALS.

T. Siddique, Northwestern University, Feinberg School of Medicine, Chicago, Illinois: Is neurodegeneration a consequence of protein in evolutionary conflict?

General Discussion

Closing Remarks

SESSION VI

Chairperson: T. Maniatis, Columbia University Medical Center, New York

Conference Room

Communicating Science

April 19–24

FUNDED BY **Boehringer Ingelheim Fonds Foundation for Basic Research in Medicine**

ARRANGED BY **S. Schedler,** Boehringer Ingelheim Fonds, Mainz, Germany
C. Walther, Boehringer Ingelheim Fonds, Mainz, Germany

The Boehringer Ingelheim Fonds (BIF) has an international program of support for PhD fellowship, and it first brought its fellows to the Banbury Center for their annual North American retreat in 2005. It has been a great pleasure to have them return, and their 2013 stay at Banbury was the sixth occasion on which they have been here. At Banbury, the fellows receive intensive instruction in matters such as giving presentations and writing papers—topics usually learned by default (and often poorly) during graduate research.

Opening Remarks and All About BIF
C. Walther, Boehringer Ingelheim Fonds, Mainz, Germany

Communication in General
N. LeBrasseur, DNA Medical Communications, New York, New York
Writing techniques and how to structure papers

Preparing and Delivering a Scientific Talk
B. Tansey, Vanderbilt University Medical Center, Nashville, Tennessee

How to Measure Success in Science
R. Lehmann, New York University School of Medicine, New York, New York

How to Design Figures
K. Ris-Vicari, Katie Ris-Vicari Graphic Design, Levitown, New York and Matt Hansen, Nature Publishing Group, New York, New York

Developing a Neuroscience Consortium

April 28–30

FUNDED BY **ISCTM and Individual Participants**

ARRANGED BY **L. Alphs,** Janssen Pharmaceuticals, Titusville, New Jersey
A. Holden, Pharmaceutical Biomedical Research, Chicago, Illinois

There has been considerable support for developing a consortium to combine existing industry databases (with the goal of including quality data from other sources as well). Given the level of interest and support, this meeting was convened to discuss the practical issues involved and what can be done to move the project forward. The topics that were reviewed included the goals for the Neuroscience Consortium; what might be the organizational structure of the Consortium and how might it relate to or even be integrated into existing organizations; the legal and intellectual hurdles that must be overcome to make this organization successful; the possible financial models for this organization; and the major milestones and timeline for the successful development of this consortium.

L. Alphs, M. Burke

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

Introduction and Outline of the Meeting: L. Alphs, Janssen Pharmaceuticals, Titusville, New Jersey and
A. Holden, Pharmaceutical Biomedical Research, Chicago, Illinois

SESSION 1: Rationale for Consortium: The Value of Big Neuroscience Clinical Data

Goal: Brainstorming on What the Precompetitive Neuroscience Data-Sharing Consortium Might Do

Brief presentations followed by brief discussions that summarize a variety of potential different uses of consortium data.

W. Potter, National Institute of Mental Health, Bethesda, Maryland: The value of big neuroscience clinical data: A perspective from NIH.

Discussion

J. Dudley, Mount Sinai School of Medicine, New York: The value of big neuroscience clinical data: A computational biologist's perspective.

Discussion

A. Cross, AstraZeneca Pharmaceuticals, Cambridge, Massachusetts: The value of big neuroscience clinical data: A drug developer's perspective.

Discussion

H. Geerts, Silico Biosciences, Philadelphia, Pennsylvania: The value of big neuroscience clinical data: A disease modeler's perspective.

Discussion

M. Arrighi, Janssen Research and Development, South San Francisco, California: (presented by Larry Alphs)

The value of big neuroscience clinical data: An epidemiologist's perspective.

Discussion

D. Meltzer, University of Chicago, Illinois: The value of big neuroscience clinical data: An economist's perspective.

Discussion

W.R. McCombie, Cold Spring Harbor Laboratory: The value of big neuroscience clinical data: A geneticist's perspective.

Discussion

S. Potkin, University of California, Irvine: The value of big neuroscience clinical data: A neuroimager's perspective.

Discussion

SESSION 2: Breakout Groups

Goal: Discuss What This Precompetitive Neuroscience Data-Sharing Consortium Might Do

Builds on ideas from the morning session and other ideas that participants may have.

Breakout Group I
Leader: R. Conley, Eli Lilly & Company, Indianapolis, Indiana
Rapporteur: H. Heimer, Schizophrenia Research Forum, Providence, Rhode Island

Breakout Group II
Leader: S. Potkin, University of California, Irvine
Rapporteur: M. Schatz, Cold Spring Harbor Laboratory

Breakout Group III
Leader: S. Romano, Pfizer, New York
Rapporteur: J. Sum, First Manhattan Company, New York

SESSION 3: Breakout Groups

Goal: Prioritize in Small Groups What This Precompetitive Neuroscience Data-Sharing Consortium Might Do Prioritization should be based on value and doability of the idea.

Switch Groups: Discuss and Build on Ideas from Other Groups
Leaders: R. Conley, S. Potkin, S. Romano
Rapporteurs: H. Heimer, M. Schatz, Joseph Sum

A. Holden, Pharmaceutical Biomedical Research, Chicago, Illinois: Ongoing Consortium Initiatives: Goals, Successes, Hurdles, Solutions, and Failures: Lessons from the Serious Adverse Event Consortium

Group Discussion

PLENARY SESSION 4: Presentation of Final Ideas and Voting on Priorities of Ideas Consortium

Chairperson: A. Vogt, Hoffmann La-Roche, Basel, Switzerland
Goal: Agree as a Plenary Group on Priorities for What This Precompetitive Neuroscience Data-Sharing Consortium Might Do
Rapporteur: H. Heimer, E. Garofalo, A. Satlin

Group Discussion and Consensus on Objectives for Direction of Consortium

PLENARY SESSION 5: Identifying and Addressing Hurdles to the Development of a Neuroscience Consortium

Goal: Learn from Persons Who Have Led Other Consortia Experienced in Bringing Similar Databases Together

D. Stephenson, Critical Path Institute, Tucson, Arizona: Ongoing consortium initiatives: Goals, successes, hurdles, solutions and failures: Lessons from CAMD.

Group Discussion

J. Rabinowitz, Bar-Ilan University, Ramat-Gan, Israel: Ongoing consortium initiatives: Goals, successes, hurdles, solutions and failures: Lessons from IMI New Med.

Group Discussion

Goal: Focus on Specific Important Hurdles and Their Solutions for Developing This Precompetitive Neuroscience Data-Sharing Consortium

J. Contreras, American University, Washington, DC: Hurdles and solutions: Legal considerations/financial models.

Group Discussion

M. Schatz, Cold Spring Harbor Laboratory: Hurdles and solutions: IT considerations.

Group Discussion

PLENARY SESSION 6

Goal: Review and Build on Ideas from April 29 on the Precompetitive Neuroscience Data-Sharing Consortium. Firmly determine if there will be further work on this effort and, if so, what the next steps will be.

L. Alphs, Janssen Pharmaceuticals, Titusville, New Jersey: Review of Day 1.

Identification of Key Consideration for Development of Precompetitive Neuroscience Data-Sharing Consortium

Mission Statement and Primary Goals

J. Sum, First Manhattan Co., New York: Financial considerations and solutions.

Next Steps

Group Discussion

Organizational Structure and Governance Considerations and Solutions
Receipt and Safety of Data
Analysis of Data
Interpretation of Data
Access to Data

Group Discussion: Identification of outstanding issues and new ideas

Immediate Next Steps and Final Summarization

Redesigning Photosynthesis: Identifying Opportunities and Novel Ideas

May 13–16

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

ARRANGED BY **S. Merchant,** University of California, Los Angeles
D. Ort, University of Illinois, Urbana

D. Ort, S. Merchant

Nearly all other biological processes on earth depend on the ability of photosynthesis to convert solar energy into chemical energy. There is a great deal of interest in the efficiency with which photosynthesis can accomplish this as it is the basis of the yield potential of both our food and bioenergy crops. Sometimes it is stated that photosynthesis is nearly 100% efficient because under ideal conditions, one photon of light can result in one photosynthetic charge separation. But in the world's best agricultural regions, only about 1% of the total solar energy that falls on the field during the growing season is stored as chemical energy in the plant materials at the end of the season. The key question discussed at this meeting was Can the efficiency of solar energy captured by photosynthesis be improved even though evolution has provided very little genetic variation in the component mechanisms of photosynthesis?

Welcoming Remarks: J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory
Workshop Introduction: D. Ort, University of Illinois, Institute for Genomic Biology, Urbana

The purpose of the short (10-min, four-slide) presentations was for the participants to introduce their relevant expertise to the other participants and provide a sense of their research questions, as well as their initial thoughts or ideas toward redesigning photosynthesis. Participants were asked to focus on their work and ideas that were relevant to the workshop and its goals.

Participant Presentations I

J. Alric, CEA Cadarache, Saint-Paul-les-Durance, France
A. Barkan, University of Oregon, Eugene
R. Croce, VU University Amsterdam, The Netherlands
M. Hanson, Cornell University, Ithaca, New York
J. Hibberd, University of Cambridge, England
D. Lindstrom, Agilent Laboratories, Santa Clara, California

Participant Presentations II

S. Merchant, University of California, Los Angeles
T. Moore, Arizona State University, Tempe
J. Moroney, Louisiana State University, Baton Rouge
K. Niyogi, University of California, Berkeley
D. Ort, University of Illinois, Institute for Genomic Biology, Urbana
M. Parry, Rothamsted Research Ltd., Hertfordshire, United Kingdom
P. Peralta-Yahya, Georgia Institute of Technology, Atlanta, Georgia
R. Prince, Exxon Mobil Research and Engineering Co., Annandale, New Jersey
K. Redding, Arizona State University, Tempe
M. Spalding, Iowa State University, Ames

Participant Presentations III

K. Van Wijk, Cornell University, Ithaca, New York
W. Vermaas, Arizona State University, Tempe
T. Yeates, University of California, Los Angeles
J. Yuan, Texas A&M University, College Station
X. Zhu, Chinese Academy of Sciences, Shanghai, China

Sectional Topic Overviews

These longer (25-min) presentations were intended to introduce and give an overview of the opportunities in the different subprocesses or components of photosynthesis.

S. Long, University of Illinois at Urbana-Champaign, Urbana, Illinois: Identifying limitations.
R. Blankenship, Washington University, St. Louis, Missouri: Optimizing/redesigning light capture.
S. von Caemmerer, Australian National University, Canberra: Optimizing/redesigning carbon reduction.
A. Weber, Heinrich–Heine University, Dusseldorf, Germany: Defeating oxygenation/improving photorespiration.
R. Bock, Max-Planck Institute of Molecular Plant, Potsdam-Golm, Germany: Synthetic biology and new tools.

Breakout Groups

Synthesis Session I: Report Back from Breakouts on Priorities for Each Goal. Reorganize breakout groups.

Synthesis Session II: Report Back from Breakouts on Priorities for Each Goal. Discussion of meeting outcomes.

Perspective from a Funding Source

K. Kahn, Bill & Melinda Gates Foundation, Seattle, Washington

Discussion of Next Steps (e.g., Publication, Proposal Initiatives)

S. von Caemmerer, B. Stillman

The Emerging Intersection between Physical Sciences and Oncology

July 14–16

FUNDED BY **USC NCI Physical Sciences in Oncology Center**

ARRANGED BY **D. Agus,** University of Southern California, Los Angeles
D. Hillis, Applied Minds, Inc., Glendale, California
P. Mallick, Stanford School of Medicine, California

This was the second occasion on which the Physical Sciences in Oncology Center came to Banbury Center to report on progress and to stimulate ideas about the challenges and solutions in the detection and treatment of cancer. As before, participants were not restricted to cancer research but included some of the foremost leaders and emerging scientists in clinical care, cancer biology, engineering, and physics. The meeting was structured to promote interactions between members of different research areas by classifying participants into two groups: Group A had a biological/clinical focus and Group B had a technology/engineering focus. Members of each group were paired with a member of the other group to identify a research project of mutual interest and a potential approach for solving it. One objective was to give junior investigators an opportunity to work with more senior investigators and get direct mentorship on how to overcome the challenges associated with working in this highly interdisciplinary field.

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

Teams

1. J. Iwasa, D. Ruderman, C. Behroozi
2. J. Sachs, A. Sharif, P. Newton
3. P. Bhatnagar, P. Macklin
4. S. Mumenthaler, M. Said, M. Padi
5. H. Karnofsky, V. Stodden, A. Naeim
6. R. Dror, D. Felsher
7. R. Judson, J. LaBaer
8. J. Mogil, P. Mallick, M. Gross

SESSION 1: Presentation of Team 1

SESSION 2: Presentations of Teams 2 and 3

SESSION 3: Presentations of Teams 4 and 5

SESSION 4: Presentations of Teams 6, 7, and 8

SESSION 5: Presentations by Teams 1 and 2

SESSION 6: Presentations by Teams 3 and 4

SESSION 7: Presentations by Teams 5, 6, 7, and 8

Telomeres and Disease

September 8–11

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

ARRANGED BY **M. Armanios,** Johns Hopkins University, Baltimore, Maryland
P. Lansdorp, University of Groningen, University Medical Centre Groningen, The Netherlands

A growing body of evidence is implicating telomeres in the pathogenesis of several important and common disorders, including pulmonary fibrosis, bone marrow failure, and diabetes. However, the underlying role of telomeres in these diverse disorders is not fully understood. This discussion meeting brought scientists and clinicians together to review and critically assess current data on how telomere dysfunction contributes to disease. Participants included scientists working on telomere biology as well as in other areas that are relevant to the study of these disorders. The goal was to forge new links between fundamental biology and telomere-mediated disorders.

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

Overviews: M. Armanios, Johns Hopkins University, Baltimore, Maryland;
P. Lansdorp, University of Groningen, University Medical Centre Groningen, The Netherlands

SESSION 1: Telomerase, Dyskeratosis Congenita, and Mouse Models

Chairperson: L. Harrington, University of Montreal, Quebec, Canada

C. Greider, Johns Hopkins University School of Medicine, Baltimore, Maryland: Short telomeres and mouse models of telomere-mediated disease.

I. Dokal, Barts & The London School of Medicine & Dentistry, London, United Kingdom: Dyskeratosis congenita and related diseases.

M. Bessler, Children's Hospital of Philadelphia, Pennsylvania: Using IPCs for the investigation of X-linked dyskeratosis congenita.

SESSION 2: Telomerase Structure, Function, and Biogenesis

Chairperson: S. Artandi, Stanford University Medical Center, California

K. Collins, University of California, Berkeley: Telomerase holoenzyme regulation.

P. Baumann, Stowers Institute for Medical Research, Kansas City, Missouri: Telomerase RNA biogenesis.

J. Chen, Arizona State University, Tempe: New mechanistic insights into the telomerase catalytic cycle.

SESSION 3: Telomere End-Protection, CST, and Disease

Chairperson: A. Bertuch, Baylor College of Medicine, Houston, Texas

V. Lundblad, Salk Institute for Biological Studies, La Jolla, California: Faithful replication of duplex telomeric DNA is necessary for telomere homeostasis.

T. Linnankivi, University of Helsinki, Finland: The clinical phenotype of Coats plus (CRMCC) syndrome.

E. Jenkinson, University of Manchester, England: Mutations in CTC1, encoding conserved telomere maintenance component 1, cause Coats plus.

C. Price, University of Cincinnati, Ohio: The multiple roles of human CST and how they may relate to human disease.

SESSION 4: DC and Bone Marrow Failure Syndromes II

Chairperson: K. Collins, University of California, Berkeley

A. Bertuch, Baylor College of Medicine, Houston, Texas: Mutations associated with very short leukocyte telomere length and early childhood disease presentation.

S. Savage, National Cancer Institute, Rockville, Maryland: Clinical and epidemiological considerations in telomere biology disorders.

J. Tolar, University of Minnesota, Minneapolis: Refining hematopoietic cell transplantation in dyskeratosis congenita: Where now, and where next?

A. Smogorzewska, Rockefeller University, New York: Fanconi anemia: DNA repair and bone marrow failure syndrome.

SESSION 5: Telomeres and Pulmonary Fibrosis

Chair: C. Price, University of Cincinnati, Cincinnati, Ohio

M. Armanios, Johns Hopkins University, Baltimore, Maryland: Telomeres and age-related lung disease.

B. Hogan, Duke University Medical Center, Durham, North Carolina: Stem cells in the adult lung and models of pulmonary fibrosis.

SESSION 6: Telomeres and Stem Cells

Chairperson: J. Sedivy, Brown University, Providence, Rhode Island

P. Lansdorp, University of Groningen, University Medical Centre, The Netherlands: Mortal and immortal stem cells.

S. Artandi, Stanford University Medical Center, California: Telomerase in stem cells and disease.

R. Reddel, Children's Medical Research Institute, Westmead, Australia: Functional role of ATRX deficiency in ALT

SESSION 7: Senescence and the DNA-Damage Response

Chairperson: A. Smogorzewska, Rockefeller University, New York

J. Sedivy, Brown University, Providence, Rhode Island: How are telomeres, cellular senescence, transposable elements and aging connected?

V. Lundblad, L. Harrington

M. Bessler, I. Dokal

F. D'Adda Di Fagagna, IFOM Foundation–FIRC Institute of Molecular Oncology Foundation, Milan, Italy: Telomeres in aging and cancer.

E. Hendrickson, University of Minnesota Medical School, Minneapolis: Escape from telomere-driven crisis is DNA ligase III-dependent.

L. Harrington, University of Montreal, Quebec, Canada: Latent implications of critically short telomeres on cellular differentiation in aging and disease.

E. Lazzerini Denchi, Scripps Research Institute, La Jolla, California: Shelterin complex mutations and genomic instability.

Conference Room

Neurobiology and Clinical Study of Rapid-Acting Antidepressants

September 15–18

FUNDED BY **Janssen Pharmaceutical Research and Development, Johnson & Johnson**

ARRANGED BY **R. Duman,** Yale University, New Haven, Connecticut
C. Zarate, National Institute of Mental Health, Bethesda, Maryland

Mood disorders affect millions of people worldwide, but a major limitation of existing pharmacotherapies is that they take weeks or months to show therapeutic effects. This lag exerts a toll on patients' well-being and ability to function and increases the already high risk of suicide. Therefore, rapid-onset pharmacological strategies with pronounced and sustained effects would have an enormous impact on public health. Recent studies have found that the drug ketamine produces antidepressant and antisuicidal effects within hours in treatment-resistant depressed patients. However, ketamine also produces psychotic-like symptoms, which limits its therapeutic use. A vigorous effort, both preclinical and clinical, has arisen to explore ketamine's mechanism of action, with an eye toward developing safer alternatives. This meeting provided an opportunity to examine the critical questions and outline the steps to developing safe rapid-acting antidepressants.

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

Introduction: R. Duman, Yale University, New Haven, Connecticut
C. Zarate, National Institute of Mental Health, Bethesda, Maryland

SESSION 1: Rapid Antidepressant Actions of NMDA Receptor Antagonists

Chairperson: H. Mayberg, Emory University School of Medicine, Atlanta, Georgia

J. Krystal, Yale University School of Medicine, New Haven, Connecticut: Overview of the clinical actions of ketamine and glutamate neurobiology.

D. Charney, Icahn School of Medicine at Mount Sinai, New York: Rapid clinical actions of ketamine.

S. Mathew, Baylor College of Medicine, Houston, Texas: Impact of ketamine on suicidality in patients with treatment-resistant depression.

C. Zarate, National Institute of Mental Health, Bethesda, Maryland: Clinical effects of ketamine and biomarkers of treatment response.

W. Drevets, Janssen Research & Development, Titusville, New Jersey: NR2B antagonists as rapid acting antidepressants.

General Discussion

SESSION 2: Rapid Actions of Muscarinic Receptor Antagonists: Mechanisms for Scopolamine and Ketamine

Chairperson: J. Krystal, Yale University School of Medicine, New Haven, Connecticut

M. Furey, National Institute of Mental Health, Bethesda, Maryland: Clinical actions of scopolamine and biomarkers of response.

C. Jones, Vanderbilt University, Nashville, Tennessee: Neurobiology and pharmacology of muscarinic receptors.

G. Sanacora, Yale University School of Medicine, New Haven, Connecticut: Regulation of glutamate/GABA metabolism by rapid antidepressants.

R. Duman, Yale University School of Medicine, New Haven, Connecticut: Synaptogenic actions of rapid-acting antidepressants.

General Discussion

SESSION 3: Neurobiology and Circuitry of Depression and Potential Rapid Antidepressant Targets

Chairperson: R. Duman, Yale University School of Medicine, New Haven, Connecticut

E. Nestler, Icahn School of Medicine at Mount Sinai, New York: Transcriptional and epigenetic mechanisms of depression.

R. Hen, College of Physicians & Surgeons, New York: Hippocampal-amygdala and related circuits in depression and anxiety.

M.-H. Han, Icahn School of Medicine at Mount Sinai, New York: VTA dopamine system and depression.

E. Castren, University of Helsinki, Finland: Isoflurane as a rapid-acting antidepressant.

G. Chen, Johnson & Johnson Pharmaceutical Research and Development, San Diego, California: Preclinical models of depression and drug development.

General Discussion

SESSION 4: Novel Rapid Antidepressant Approaches I: Glutamatergic Mechanisms and Targets

Chairperson: E. Nestler, Icahn School of Medicine at Mount Sinai, New York

D. Bredt, Johnson & Johnson Pharmaceutical Research & Development, San Diego, California: Overview of glutamatergic receptor synaptic mechanisms.

J. Witkin, Lilly Research Laboratories, Indianapolis, Indiana: AMPA receptor potentiation: Potential impact on TRD.

E. Nestler

H. Mayberg

J. Moskal, Northwestern University, Evanston, Illinois: GLYX-13, a novel NMDA receptor modulator with rapid onset and long-lasting antidepressant effects in humans without ketamine-like side effects.

S. Chaki, Taisho Pharmaceutical Co, Ltd., Saitama, Japan: mGlu2/3 receptor antagonists as antidepressants.

P. Skolnick, National Institute on Drug Abuse, Bethesda, Maryland: AMPA receptor potentiators as antidepressants.

General Discussion

SESSION 5: Novel Rapid Antidepressant Approaches II: Drug Development and Clinical Study Design

Chairperson: C. Zarate, National Institute of Mental Health, Bethesda, Maryland

H. Mayberg, Emory University School of Medicine, Atlanta, Georgia: DBS as a rapid antidepressant treatment and neurobiological mechanisms.

W. Bunney, University of California, Irvine: Circadian rhythms, clock genes, and sleep deprivation therapy in depression.

J. Heemskerk, National Institute of Mental Health, Bethesda, Maryland: Funding drug development.

M.R. Trivedi, University of Texas Southwestern Medical Center, Dallas: Integrating biomarkers in clinical research.

M. Fava, Massachusetts General Hospital, Boston: Study design and outcome measures for the NIMH RAPID studies.

Closing Discussion and Summary

Plant Reproduction

September 22–25

FUNDED BY **CSHL/DuPont Pioneer Joint Collaborative**

ARRANGED BY **R. Martienssen,** Cold Spring Harbor Laboratory
R. Meeley, DuPont Pioneer, Johnston, Iowa

This was the annual meeting of the collaborative project between the plant science group at Cold Spring Harbor Laboratory and scientists at DuPont Pioneer. The goals of this meeting were to explore the latest advances in our understanding of sexual and asexual reproduction in crop and model plant species and to drive discussions on current research addressing genetic, epigenetic, and population-based approaches to manipulating key mechanisms in plant reproductive biology. As usual, one day was devoted to presentations from speakers outside the collaboration.

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

Introduction: R. Meeley, DuPont Pioneer, Johnston, Iowa
R. Martienssen, Cold Spring Harbor Laboratory

SESSION 1: Data Mining in Expression Networks

Chairperson: R. Meeley, DuPont Pioneer, Johnston, Iowa

Y.K. Lee, Cold Spring Harbor Laboratory: The *Arabidopsis* root miRNA regulatory network supports functional characterization of transcription factors involved in development and environmental response.

C. Liseron-Monfils, Cold Spring Harbor Laboratory: The dynamic of gene coexpression within *Arabidopsis* miRNA-based genetic network during plant development and response to stresses.

A. Eveland, Cold Spring Harbor Laboratory: Systems approaches in maize inflorescence architecture and drought.

SESSION 2: Somatic Patterning and Small RNA

Chairperson: M. Cigan, Pioneer Hi-Bred International, Johnston, Iowa

K. Petsch, Cold Spring Harbor Laboratory: Hierarchical *DICER* activity in maize triggers alternate processing of tasiARF target transcripts.

M. Timmermans, Cold Spring Harbor Laboratory: Patterning properties of mobile small RNAs.

Y. Plavskin, Cold Spring Harbor Laboratory: Regulation of the auxin response by an ancient small RNA pathway.

SESSION 3: Genetic Dissection of Inflorescence Development

Chairperson: L. Perugini, DuPont Pioneer, Johnston, Iowa

B. ll Je, Cold Spring Harbor Laboratory: Finding the function of *fasciated ear3.*

M. Pautler, Cold Spring Harbor Laboratory: *FASCIATED EAR4:* Function and targets.

D. Jackson, Cold Spring Harbor Laboratory: Update on *RAMOSA3* in maize and *Arabidopsis.*

SESSION 4: Targeted Molecular and Genetic Strategies

Chairperson: D. Jackson, Cold Spring Harbor Laboratory

L. Perugini, DuPont Pioneer, Johnston, Iowa: Characterization of ear trait mutants for increasing yield in elite maize germplasm.

B. Li, DuPont Experimental Station, Wilmington, Delaware: Understanding the molecular mechanisms of gene–background interactions: Two case studies.

M. Cigan, Pioneer Hi-Bred International, Johnston, Iowa: Targeted genome modification of plant fertility genes using double-strand-break reagents.

M. Williams, DuPont Experimental Station, Wilmington, Delaware: The interaction of genetics and mutagenesis.

SESSION 5: A Landscape of Reproductive Strategies

Chairperson: S. Lawit, DuPont Pioneer, Johnston, Iowa

M. Singh, DuPont Pioneer, Johnston, Iowa: Genetic and epigenetics of apomixis in maize.

A. Schnittger, Institut de Biologie Moleculaire des Plantes, Strasbourg, France: Control of germline entry in *Arabidopsis.*

T. Dresselhaus, Universitat Regensburg, Germany: Fertilization mechanisms and early embryogenesis in maize.

SESSION 6: Developmental and Reproductive Outcomes of Auxin Signaling

Chairperson: B. Li, DuPont Pioneer, Wilmington, Delaware

P. McSteen, University of Missouri, Columbia: Role of auxin in maize inflorescence development.

M. Evans, Carnegie Institution for Science, Stanford, California: Mutant analysis of maize antipodal cells and auxin signaling.

SESSION 7: Epigenetics that Pattern Reproductive Boundaries

Chairperson: M. Singh, DuPont Pioneer, Johnston, Iowa

C. Kohler, Swedish University of Agriculture Science, Uppsala, Sweden: Epigenetic mechanisms establishing interploidy and interspecies hybridization barriers in the endosperm.

R. Martienssen, Cold Spring Harbor Laboratory: Reprogramming heterochromatin in the germline and its consequences.

SESSION 8: Technical Approaches to Recombination

Chairperson: R. Martienssen, Cold Spring Harbor Laboratory

G. May, DuPont Pioneer, Johnston, Iowa: Genomic approaches to recombination.

W. Pawlowski, Cornell University, Ithaca, New York: The landscape of meiotic recombination in maize.

A. Eveland

B. Li, D. Jackson

R. Mercier, INRA Centre de Versailles-Grignon, Versailles, France: What limits meiotic recombination?

F. de Sousa Borges, Cold Spring Harbor Laboratory: The pollen methylome and implications for epiallele formation.

SESSION 9: Genetic and Epigenetic Pathways in Flowering and Reproductive Success

Chairperson: M. Komatsu, DuPont Pioneer, Wilmington, Delaware

Z. Lippman, Cold Spring Harbor Laboratory: Fine-tuning flowering to boost yield.

C. Xu, Cold Spring Harbor Laboratory: The TMF-BOP complex directs inflorescence architecture in tomato.

C. MacAlister, Cold Spring Harbor Laboratory: From meristems to pollen tubes to protonema: An unknown gene family with diverse functions in plant development.

SESSION 10: Development of Apomictic Strategies

Chairperson: M. Timmermans, Cold Spring Harbor Laboratory

R. Herridge, Cold Spring Harbor Laboratory: The role of argonautes in reproductive strategies in *Arabidopsis.*

S. Lawit, DuPont Pioneer, Johnston, Iowa: Research frontiers of plant female reproductive strategies in *Arabidopsis.*

M. Williams, DuPont Stine-Haskell Research Center, Newark, Delaware: Self-reproducing hybrid technology in maize.

Meeting Wrap-Up

Science of Pancreatic Cancer

September 29–October 1

FUNDED BY **MCJ Amelior Foundation and Kotumba Capital Management LLC**

ARRANGED BY **R. Evans,** Salk Institute for Biological Studies, La Jolla, California
W. Isacoff, University of California, Los Angeles
D. Tuveson, Cold Spring Harbor Laboratory

Recent findings in pancreatic cancer science and medicine demonstrate that both neoplastic cell genetic changes and distinct features of the tumor microenvironment may serve as therapeutic vulnerabilities in this malignancy. This meeting focused on the role of the stroma in modulating therapeutic responses and the development of new dependency pathways. Topics reviewed included vitamin D and pancreatic stellate cell activation; survival cues in the tumor microenvironment as major causes of drug resistance; methods to develop a tissue bank of the tumor microenvironment and cancer cells; and the role of genomics in addressing this disease. The meeting concluded with a discussion intended to help identify one or two important areas worthy of large-scale additional investigation.

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

SESSION 1: Pancreatic Stromal Cells and Opportunities

Chairperson: D. Tuveson, Cold Spring Harbor Laboratory

R. Kalluri, University of Texas, MD Anderson Cancer Center, Houston: Stromal biology in PDAC.

D. Fearon, CRUK Cambridge Institute, United Kingdom: FAP+ cells and immune suppression.

M. Egeblad, Cold Spring Harbor Laboratory: Imaging the PDAC stroma.

SESSION 2: Pancreatic Stroma and Manipulation

Chairperson: D. Tuveson, Cold Spring Harbor Laboratory

R. Evans, Salk Institute for Biological Studies, La Jolla, California: PSCs and vitamin D.

M. Hollingsworth, University of Nebraska Medical Center, Omaha: The best targets in PDAC.

G. Wahl, Salk Institute for Biological Studies, La Jolla, California: Stromal and epithelial approaches to pancreatic cancer.

General Discussion

SESSION 3: Neoplastic Cells and Therapeutic Opportunities in PDAC

Chairperson: R. Evans, Salk Institute for Biological Studies, La Jolla, California

T. Hunter, Salk Institute for Biological Studies, La Jolla, California: Secreted proteins that mediate cross-talk between stellate cells and tumor cells.

A. Maitra, University of Texas, MD Anderson Cancer Center, Houston: Triple metabolism therapy in PDAC.

K. Olive, Columbia University, New York: Targeting ROS detoxification in pancreatic cancer.

SESSION 4: Neoplastic Cells and Therapeutic Opportunities

Chairperson: R. Evans, Salk Institute for Biological Studies, La Jolla, California

A. Lowy, University of California, San Diego, Moores Cancer Center, La Jolla, California: Targeting RON in PDAC.

H. Crawford, Mayo Clinic Florida, Jacksonville, Florida: Signaling cascades as targets in PDAC.

S. Muthuswamy, University of Toronto, Ontario, Canada: A new model system for PDAC.

Summary Discussion, What Have We Heard?
P. Philip, Karmanos Cancer Center, Detroit, Michigan
B. Stillman, Cold Spring Harbor Laboratory

SESSION 5: Additional Opportunities in PDAC

Chairperson: W. Isacoff, University of California, Los Angeles

C. Iacobuzio-Donahue, Johns Hopkins University, Baltimore, Maryland: Moving genetic targets in PDAC.

N. Bardeesy, Massachusetts General Hospital Cancer Center, Boston: Role of MiT proteins in metabolic reprogramming in pancreatic cancer.

S. Leach, Johns Hopkins University, Baltimore, Maryland: Targeting PanIN initiation and progression.

SESSION 6: Final Discussion and Next Steps

Chairperson: W. Isacoff, University of California, Los Angeles

P. Philip, Karmanos Cancer Institute, Detroit, Michigan: Status of clinical trials.

T. Donahue, David Geffen School of Medicine, Los Angeles, California: Translational PET imaging to guide chemotherapy in human pancreatic cancer.

Final Meeting Summary: Is the Science Ready for Transformative Clinical Efforts?
W. Isacoff, University of California, Los Angeles
R. Evans, Salk Institute for Biological Studies, La Jolla, California
D. Tuveson, Cold Spring Harbor Laboratory

T. Hunter

Biguanides and Neoplasia

October 6–9

FUNDED BY **Oliver Grace Cancer Fund**

ARRANGED BY **M. Pollak,** McGill University, Montreal, Quebec, Canada
K. Struhl, Harvard Medical School, Boston, Massachusetts

Interest in potential roles of biguanides such as metformin in treatment and/or prevention of neoplastic disease continues to increase since the topic was last discussed at Banbury in 2011. Participants in the 2013 meeting discussed the nature of the primary site of action in mitochondria, the alterations in cellular energetics and metabolism caused by biguanides, and the genetic factors that influence these effects. Additionally, the effects of biguanides at the whole-organism level were reviewed, including modulation of both inflammatory responses and the endocrine environment. An important discussion centered on strategies for optimizing drug exposure to target tissues, which may differ from those important in diabetes treatment. Finally, the use of preclinical findings to optimize the design of future trials was reviewed.

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

Introduction: K. Struhl, Harvard Medical School, Boston, Massachusetts

Overview of Progress Since Last Meeting: M. Pollak, McGill University, Montreal, Quebec, Canada

SESSION 1

Chairperson: M. Pollak, McGill University, Montreal, Quebec, Canada

J. Hirst, The Medical Research Council, The Wellcome Trust/MRC Building, Cambridge, United Kingdom: Effects of biguanides on mitochondrial complex I.

M. Schwab, University Hospital of Tuebingen, Stuttgart, Germany: Metformin and drug disposition: Update and future perspectives.

B. Kahn, Beth Israel Deaconess Medical Center, Boston, Massachusetts: AMPK and the regulation of food intake, body weight, and metabolism.

SESSION 2

Chairperson: K. Struhl, Harvard Medical School, Boston, Massachusetts

L. Cantley, Weill Cornell Medical College, New York: AMPK and cancer.

R. Shaw, Salk Institute for Biological Studies, La Jolla, California: LKB1/STK11 genotype dictates therapeutic response to phenformin.

J. Pouyssegur, University of Nice, France: Targeting glycolysis (lactate transporters) sensitizes tumor cells to phenformin.

M. Pollak, McGill University, Montreal, Canada: Serine deficiency sensitizes neoplastic cells to phenformin.

K. Birsoy, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts: Metabolic liabilities of cancer cells to nutrient limitation.

SESSION 3

Chairperson: R. Shaw, Salk Institute for Biological Studies, La Jolla, California

M. Stampfer, Harvard University, Brigham and Women's Hospital, Boston, Massachusetts: Metformin and prostate cancer prevention.

N. Fleshner, Princess Margaret Hospital, Toronto, Canada: Rationale for metformin in prostate cancer.

C. Dang, University of Pennsylvania, Philadelphia: Activities of biguanides and metabolic inhibitors in human pancreatic cancer xenografts.

N. Hay, University of Illinois, Chicago: Targeting glucose metabolism for cancer therapy

P. Puigserver, Dana-Farber Cancer Institute, Boston, Massachusetts: Therapeutic implications of metabolic and energy flexibility in melanoma tumors.

M. Keiser, SeaChange Pharmaceuticals, Inc. San Francisco, California: Prediction and testing of a new target for metformin with a potential role in neoplasia.

H. Udono, Okayama University, Japan: Metformin-induced reversion of immune-exhaustion in tumor microenvironment.

SESSION 4

Chairperson: R. Jones, McGill University, Montreal, Quebec, Canada

J. Schlessinger, Yale University, New Haven, Connecticut: Targeting receptor tyrosine kinases.

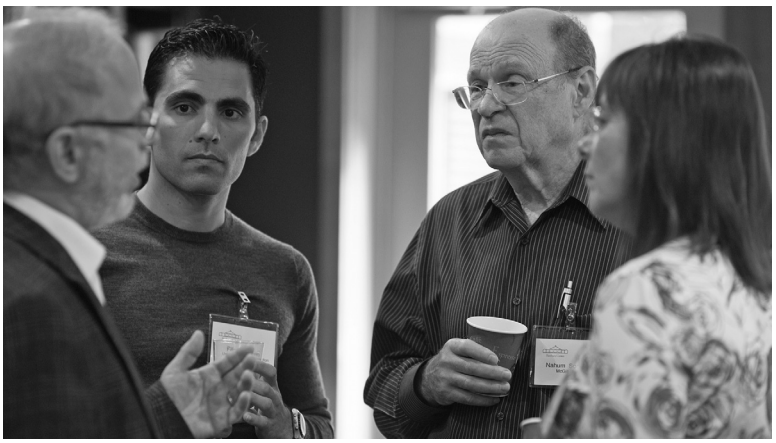
K. Struhl, David Geffen School of Medicine, Los Angeles, California: Metformin mediates anticancer effects by inhibiting the inflammatory pathway.

J.D. Watson, Cold Spring Harbor Laboratory: Exercise vs. metformin.

K. Vousden, Beatson Institute, Glasgow, United Kingdom: Regulation of metabolism through the p53 pathway.

G. Thomas, University of Cincinnati, Ohio: Metformin in the treatment of HCC?

N. Sonenberg, McGill University, Montreal, Quebec, Canada: Translational control of mitochondria function via mTOR.



M. Pollak, F. Cabreiro, N. Sonenberg, K. Vousden

J. Hirst

R. Kalluri, MD Anderson Cancer Center, Houston, Texas: Designing rational preclinical combination trials for pancreatic cancer (PDAC).

SESSION 5

Chairperson: K. Vousden, Beatson Institute, Glasgow, United Kingdom

P. Dennis, Johns Hopkins Bayview Medical Center, Baltimore, Maryland: Mechanisms of chemoprevention by metformin.

B. Zheng, Harvard Medical School, Charlestown, Massachusetts: Targeting AMPK signaling in melanoma.

G. Ferbeyre, University of Montreal, Canada: Metformin and the NF-κB pathway.

M. VanderHeiden, Massachusetts Institute of Technology, Cambridge: Understanding tumor metabolism in vivo: Implications for use of metformin to treat cancer.

F. Cabreiro, University College London, United Kingdom: Biguanides regulate microbial function to modulate host health and lifespan.

Lustgarten Foundation Scientific Meeting

October 21–22

FUNDED BY **Lustgarten Foundation for Pancreatic Cancer, Bethpage, New York**

ARRANGED BY **M. McCurragh,** Lustgarten Foundation for Pancreatic Cancer, Bethpage, New York

This meeting provided an opportunity for investigators supported by the Lustgarten Foundation to meet and to present and discuss their research. The goals of the meeting were to update the Lustgarten Foundation research community of progress in the laboratory, to evaluate performance and provide feedback for improvement, and to establish and strengthen collaborations between groups and brainstorm new ideas to push the field forward.

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

Introduction: R. Vizza, Lustgarten Foundation for Pancreatic Cancer, Bethpage, New York
D. Tuveson, Cold Spring Harbor Laboratory

Key Note Speaker: B. Vogelstein, Johns Hopkins University School of Medicine, Baltimore, Maryland

PRECLINICAL GROUP

H.C. Manning, Vanderbilt University Institute of Imaging Science, Nashville, Tennessee
Q. Nguyen, University of California, San Diego, La Jolla
S. Thorne, University of Pittsburgh, Pennsylvania
S. Hingorani, Fred Hutchinson Cancer Research Center, Seattle, Washington

General Discussion

Keynote Speaker: Cold Spring Harbor Laboratory

CONSORTIUM PANEL 1

S. Lowe, Memorial Sloan-Kettering Cancer Center, New York

C. Castro, Harvard University Medical School, Boston, Massachusetts
B. Wolpin, Dana Farber Cancer Institute, Boston, Massachusetts

General Discussion

BASIC GROUP 1

D. Fearon, CRUK Cambridge Institute, United Kingdom
G. Miller, New York University Langone Medical Center
E. O'Reilly, Memorial Sloan-Kettering Cancer Center, New York

General Discussion

BASIC GROUP 2

D. Bar-Sagi, New York University School of Medicine, New York
A. Kimmelman, Dana-Farber Cancer Institute, Boston, Massachusetts
M. Egeblad, Cold Spring Harbor Laboratory

General Discussion

BASIC GROUP 3

J.J. Yeh, University of North Carolina, Chapel Hill
T. Wang, Columbia University, New York

General Discussion

CLINICAL GROUP

H. Degani, Weizmann Institute of Science, Rehovot Israel
J. Fleming, MD Anderson Cancer Center, Houston, Texas

General Discussion

CONSORTIUM PANEL 2

C. Der, University of North Carolina, Chapel Hill
T. Van Dyke, Frederick National Laboratory for Cancer, Frederick, Maryland
S. Fesik, Vanderbilt University School of Medicine, Nashville, Tennessee

General Discussion

Meeting Summary and Future Goals
D. Tuveson, Cold Spring Harbor Laboratory

J. Watson, D. Tuveson, R. Vizza

Q. Nguyen

Ovarian Cancer: Developing Research-Based Public Messaging on Early Detection and Screening

October 23–25

FUNDED BY **Ovarian Cancer Research Fund**

ARRANGED BY **J. Boyd,** Fox Chase Cancer Center, Philadelphia, Pennsylvania
A. Moran, Ovarian Cancer Research Fund, New York
M. Seiden, McKesson Specialty Health, Woodlands, Texas

M. Seiden, A. Moran

Messages to the public about ovarian cancer should accurately reflect what research results currently demonstrate, as well as what might reasonably be expected in the near term. When the public talks about ovarian cancer and ovarian cancer research, much emphasis is placed on early detection of the disease, as well as symptoms as a means of saving lives. In practice, the matter is more complicated, depending on the type of cancer, the efficacy of the screening, and the consequences of false positives. The UK Collaborative Trial of Ovarian Cancer Screening is under way, designed to provide firm data that can be used as the basis for assessing the value of current methods of early detection of ovarian cancer. The findings of these trials will have a major impact on the ovarian cancer community. This meeting was held to review the current status of ovarian cancer screening, to discuss action that might be taken for either positive or negative results of the UKCTOCS study, and to use these discussions as the basis for developing clearly defined messages that can help lay public understand the implications of the findings.

Welcoming Remarks: J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory
A. Moran, Ovarian Cancer Research Fund, New York

Introduction: Defining the Problem, What We Hope to Accomplish
J. Boyd, Fox Chase Cancer Center, Philadelphia, Pennsylvania
M. Seiden, McKesson Specialty Health, Woodlands, Texas

SESSION 1: State of Science

J. Boyd, Fox Chase Cancer Center, Philadelphia, Pennsylvania: Whence epithelial ovarian carcinoma?
N. Urban, Fred Hutchinson Cancer Research Center, Seattle, Washington: Symptoms index and multimodal screening: Using novel markers to improve screening performance.
K. Lu, MD Anderson Cancer Center, Houston, Texas: MD Anderson Study: A stage-2 Ovarian cancer screening strategy using the risk of ovarian cancer algorithm (ROCA) identifies early-stage incident cancers and demonstrates high positive predictive value.
I. Jacobs, University of Manchester, United Kingdom: UKCTOCS update.
U. Menon, University College London, United Kingdom: Time series algorithms: What can we learn from UKCTOCS.
S. Skates, Massachusetts General Hospital, Boston: ROCA: Development and implementation in screening trials.
S. Narod, Women's College Research Institute, Toronto, Canada: Perspectives for screening for ovarian cancer.

SESSION 2: Defining Benefit

K. Trivers, Centers for Disease Control, Atlanta, Georgia: A public health approach to understanding ovarian cancer.
M. Ebell, University of Georgia, Athen, Georgia: The US Preventive Services Task Force and Ovarian Cancer Screening

Group Discussion: Provocative Questions
Moderators: J. Boyd, Fox Chase Cancer Center, Philadelphia, Pennsylvania
M. Seiden, McKesson Specialty Health, Woodlands, Texas

Day-One Recap: Group Discussion
Moderators:
J. Boyd, Fox Chase Cancer Center, Philadelphia, Pennsylvania
M. Seiden, McKesson Specialty Health, Woodlands, Texas

Concluding Discussion

U. Menon, S. Skates

Enhancer Biology in Health and Disease

October 27–30

FUNDED BY **Oliver Grace Cancer Fund**

ARRANGED BY **J. Bradner,** Dana-Farber Cancer Institute, Boston, Massachusetts
J. Wysocka, Stanford School of Medicine, California
R. Young, Whitehead Institute, MIT, Cambridge, Massachusetts

There has been rapid progress in identifying transcriptional regulatory elements and the factors that occupy them. Disease-associated sequence variation occurs in some of these regulatory elements and in the factors that bind them. This meeting brought together experts in enhancer biology to discuss the roles of regulatory elements and factors in control of gene expression programs and their impact on human health and disease.

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

SESSION 1: Enhancers and Chromatin Folding

Chairperson: J. Bradner, Dana-Farber Cancer Institute, Boston, Massachusetts

R. Young, Whitehead Institute, MIT, Cambridge, Massachusetts: Super-enhancers.

B. Ren, University of California, San Diego: Functional relationship between DNA looping and enhancer activities.

J. Dekker, University of Massachusetts, Worcester: Chromosome folding and long-range gene regulation.

M. Merkenschlager, MRC Clinical Sciences Centre, Imperial College London, United Kingdom: Cohesin and the regulation of gene expression.

V. Corces, Emory University, Atlanta, Georgia: The role of architectural proteins in organizing the 3D architecture of the genome.
W. Bickmore, University of Edinburgh, Scotland: Do enhancers function in compact chromatin domains?

General Discussion

SESSION 2: Enhancer Dynamics

Chairperson: E. Furlong, EMBL, Heidelberg, Germany
M. Levine, University of California, Berkeley: Enhancer dynamics in the *Drosophila* embryo.
J. Wysocka, Stanford School of Medicine, California: Enhancer regulation in development.
K. Zaret, Perelman School of Medicine, Philadelphia, Pennsylvania: Creating active enhancers.

SESSION 3: Enhancers in Disease Part 1: Genomic Variation

Chairperson: J. Bradner, Dana-Farber Cancer Institute, Boston, Massachusetts
M. Maurano, University of Washington, Seattle: Regulatory variation and human disease.
S. Parker, National Institutes of Health, Bethesda, Maryland: Stretch enhancers drive cell-specific gene regulation and harbor human disease variants.
P. Scacheri, Case Western Reserve University School of Medicine, Cleveland, Ohio: Combinatorial effects of multiple enhancer variants in common disease.

General Discussion

SESSION 4: Enhancers in Disease Part II: Coactivator Function

Chairperson: R. Young, Whitehead Institute, MIT, Cambridge, Massachusetts
J. Bradner, Dana-Farber Cancer Institute, Boston, Massachusetts: Disrupting enhancer function to discover and downregulate cancer dependencies.
C. Vakoc, Cold Spring Harbor Laboratory: Targeting coactivator proteins in acute myeloid leukemia.

SESSION 5: Large-Scale Functional Analysis

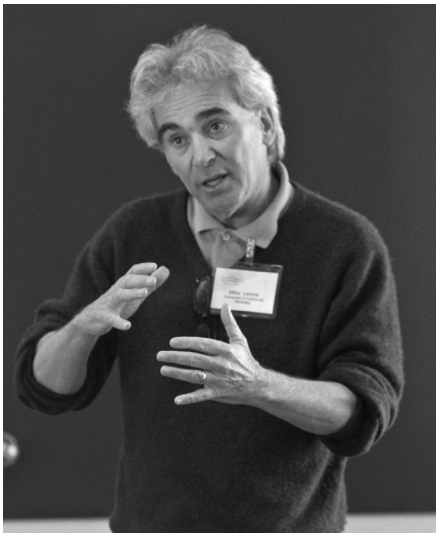
Chairperson: B. Ren, University of California, San Diego
A. Stark, Research Institute of Molecular Pathology, Vienna, Austria: Decoding transcriptional regulatory sequences.
M. Bulyk, Brigham & Women's Hospital, Boston, Massachusetts: Highly parallel enhancer assays in whole *Drosophila* embryos.
B. Bernstein, Broad Institute, Charlestown, Massachusetts: Manipulating *cis*-element landscapes in human cells.

General Discussion

SESSION 6: Enhancer Factors And Function

Chairperson: M. Levine, University of California, Berkeley
J. Zeitlinger, Stowers Institute for Medical Research, Kansas City, Missouri: Dissecting transcription factor binding at *Drosophila* enhancers using ChIP-exo.
G. Crabtree, Stanford University School of Medicine, California: ATP-dependent chromatin remodeling and enhancer function.

J. Dekker, K. Zaret



M. Levine

D. Odom, University of Cambridge, United Kingdom: Insights into mammalian enhancers from comparative functional genomics.

SESSION 7: Developmental Mechanisms

Chairperson: J. Wysocka, Stanford School of Medicine, California

E. Furlong, EMBL, Heidelberg, Germany: Temporal properties of enhancer activity during development.

T. Maniatis, Columbia University Medical Center, New York: Generation of cell surface diversity through stochastic enhancer/promoter interactions.

S. Lomvardas, University of California, San Francisco: Synergistic action of distant enhancers specifies singular olfactory receptor expression.

General Discussion

SESSION 8: Enhancers and Noncoding RNA

Chairperson: M. Bulyk, Brigham & Women's Hospital, Boston, Massachusetts

R. Shiekhattar, Wistar Institute, Philadelphia, Pennsylvania: Biogenesis and mechanism of action of enhancer RNAs.

M.G. Rosenfeld, University of California, San Diego: Nuclear receptor and IncRNA regulation of enhancer function.

J. Rinn, Broad Institute of MIT and Harvard, Cambridge, Massachusetts: Linking RNA to nuclear architecture.

Concluding Discussion: Challenges to Developing Therapies That Target Enhancer Function in Disease

INK4/ARF Network

November 12–15

FUNDED BY **Pfizer, Inc.**

ARRANGED BY **D. Beach,** University of London, United Kingdom
N.E. Sharpless, University of North Carolina, Chapel Hill
C.J. Sherr, St. Jude Children's Research Hospital, Memphis, Tennessee

This meeting celebrated the 20th anniversary of the discovery of the *INK4/ARF* locus encoding three tumor suppressor proteins that coordinate signaling of the CDK4/6-retinoblastoma (RB) and MDM2-p53 pathways. Disruption of this circuitry, frequently by deletion or silencing of *INK4/ARF*, is a hallmark of many cancers. The *INK4/ARF* locus may have evolved to physiologically restrict the self-renewal capacities and numbers of stem and progenitor cells with the attendant consequence of limiting tissue regenerative capacity, particularly as animals age. In accord with this concept, altered regulation of the *INK4/ARF* locus has been implicated in age-associated diseases in humans by unbiased, genome-wide analyses. Participants in the meeting reviewed a wide-ranging set of issues relating to the evolution and biology of the locus, and its implications for therapies.

J. Watson, D. Beach, K. Knudsen

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

Historical Overview: C. Sherr, St. Jude Children's Research Hospital, Memphis, Tennessee

SESSION 1: Signaling through the RB Pathway

Chairperson: G. Peters, CRUK London Research Institute, United Kingdom

J. Lees, Koch Institute, MIT, Cambridge, Massachusetts: Are Ink4, CycD/K4, and Rb mutations synonymous in tumorigenesis?

J. Sage, Stanford University Medical Center, California: The RB gene family in cell cycle control and cancer.

J.A. Diehl, University of Pennsylvania, Philadelphia: Dysregulation of D-type cyclins in cancer.

J. Bartek, Danish Cancer Society, Copenhagen, Demark: INK4/ARF and the DNA-damage response as a barrier to cancer progression.

General Discussion

SESSION 2: New Approaches to Cancer Treatment

Chairperson: N. Sharpless, Lineberger Comprehensive Center, Chapel Hill, North Carolina

K. Knudsen, Thomas Jefferson University, Philadelphia, Pennsylvania: Translating alterations of the p16/RB locus to the clinic: Prostate cancer.

M. Gillison, Ohio State University, Columbus: p16 and prognosis of head and neck cancer.

G. Shapiro, Harvard Medical School, Boston, Massachusetts: Clinical development of selective CDK4/6 inhibitors.

K. Arndt, Pfizer Worldwide Research & Development, Pearl River, New York: Palbociclib inhibition of CDK4/6 as a treatment for cancer.

General Discussion

SESSION 3: INK4/ARF and Aging

Chairperson: M. Serrano, Spanish National Cancer Research Center, Madrid, Spain

N. Sharpless, University of North Carolina, Chapel Hill: p16, aging, and cancer.

C. Bishop, Barts & The London School of Medicine, London, United Kingdom: p16 and senescence.

J.D. Watson, Cold Spring Harbor Laboratory: RAS, ROS, PTEN, and senescence.

C. Burd, Ohio State University, Columbus: Reporter model for p16 regulation.

J. van Deursen, Mayo Clinic, Rochester, Minnesota: p16-positive senescent cells in aging and age-related disease

SESSION 4: Senescence Networks and Development

Chairperson: J. Sage, Stanford University Medical Center, California

M. Serrano, Spanish National Cancer Research Center, Madrid, Spain: INK4/ARF locus: Developmental senescence and in vivo reprogramming.

S. Lowe, Memorial Sloan-Kettering Cancer Center, New York: New insights into the p53 tumor suppressor networks.

D. Peeper, Netherlands Cancer Institute, Amsterdam, The Netherlands: p16: A smoking gun in melanoma senescence.

S. Skapek, University of Texas Southwestern Medical Center, Dallas: Insights into Arf biology from studying blind mice.

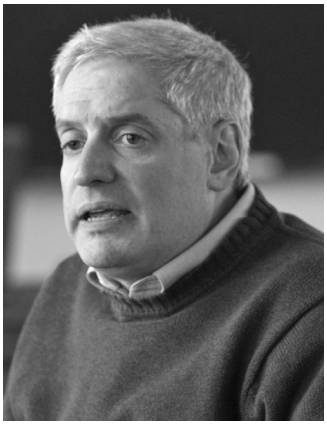
General Discussion

SESSION 5: Regulation of INK4/ARF Gene Expression

Chairperson: J. Lees, Koch Institute, MIT, Cambridge, Massachusetts

G. Peters, CRUK London Research Institute, London, United Kingdom: Polycomb regulation of INK4a.

A. Bracken, Trinity College, Dublin, Ireland: Polycomb regulation of the INK4/ARF locus.



G. Shapiro

J. Lees

J. Gil, MRC Clinical Sciences Centre, London, United Kingdom: Regulation of INK4/ARF by SWI/SNF and other chromatin modifiers.

A. Mills, Cold Spring Harbor Laboratory: Chd5-mediated regulation of the Ink4/Arf tumor suppressor network.

Y. Xiong, University of North Carolina, Chapel Hill: Epigenetic regulation of p16 and Arf.

Closing Remarks

Sammis, Winter 2013

The Adolescent Brain

December 3–5

FUNDED BY **The Allen Institute for Brain Science, the Lieber Institute for Brain Development, the National Institute on Alcohol Abuse and Alcoholism, and the National Institute of Mental Health**

ARRANGED BY **J. Giedd,** National Institute of Mental Health, Bethesda, Maryland
H. Heimer, Schizophrenia Research Forum, Providence, Rhode Island
E. Lein, Allen Institute for Brain Science, Seattle, Washington
N. Sestan, Yale University School of Medicine, New Haven, Connecticut

It has long been noted that many psychiatric disorders first make their appearance in adolescence and the transition to adulthood. Adolescence is a time of great developmental change in the human brain, and it is becoming clear that the origins of at least some of these disorders lie in the failure of normal brain development. Modern neuroscience has revealed a great deal about prenatal and early postnatal human brain development, but it has not provided much detail about later stages of neurodevelopment. This meeting surveyed the state of knowledge about normal adolescent brain and behavior and the apparent special vulnerability of the adolescent brain to mental disorders. The most recent data were critically reviewed with the aim of producing an integrated account that will point out the significant gaps in our knowledge.

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

Workshop Introduction: H. Heimer, Schizophrenia Research Forum, Providence, Rhode Island

SESSION 1: Overviews

Chairperson: H. Heimer, Schizophrenia Research Forum, Providence, Rhode Island

T. Paus, Rotman Research Institute, University of Toronto, Ontario, Canada: Adolescent brain development.

K. Mirnics, P. Rakic

C. Colantuoni, D. Weinberger

B.J. Casey, Sackler Institute, Weill Cornell Medical College, New York; Adolescent behavioral development.
J. Giedd, National Institute of Mental Health, Bethesda, Maryland: Mental illness in adolescence.
D. Weinberger, Lieber Institute for Brain Development, Baltimore, Maryland: Developmental biology and psychopathology.

SESSION 2: Short Presentations A

Chairperson: N. Sestan, Yale University School of Medicine, New Haven, Connecticut

P. Schmidt, National Institute of Mental Health, Bethesda, Maryland
E. Sowell, University of Southern California, Los Angeles
J. Tollkuhn, University of California, San Francisco
B. Luna, University of Pittsburgh, Pennsylvania
N. Tottenham, University of California, Los Angeles
Z.J. Huang, Cold Spring Harbor Laboratory

Key Issues

SESSION 3: Short Presentations B

Chairperson: E. Lein, Allen Institute for Brain Science, Seattle, Washington
C. Sisk, Michigan State University, East Lansing
R. Gur, Perelman School of Medicine, Philadelphia, Pennsylvania
L. Spear, Binghamton University, New York
I. Gotlib, Stanford University, California
F. Lee, Weill Cornell Medical College, New York

Key Issues

SESSION 4: Short Presentations C

Chairperson: J. Giedd, National Institute of Mental Health, Bethesda, Maryland
P. Rakic, Yale University School of Medicine, New Haven, Connecticut
K. Mirnics, Vanderbilt University, Nashville, Tennessee
C. Colantuoni, Lieber Institute for Brain Development, Baltimore, Maryland
E. Lein, Allen Institute for Brain Science, Seattle, Washington
N. Sestan, Yale University School of Medicine, New Haven, Connecticut
P. Mitra, Cold Spring Harbor Laboratory

Key Issues

SESSION 5: Revisiting Key Issues

Chairperson: J. Giedd, National Institute of Mental Health, Bethesda, Maryland

SESSION 6: Discussion of Next Steps (e.g., Publication, Proposal Initiatives)

Chairperson: N. Sestan, Yale University School of Medicine, New Haven, Connecticut

Psychiatric Genomics: Current Status, Future Strategies

December 8–11

FUNDED BY **The Stanley Research Fund**

ARRANGED BY **W.R. McCombie,** Cold Spring Harbor Laboratory
A. Palotie, University of Helsinki, Finland

It has been difficult to find the genes and gene loci underlying psychiatric and other complex disorders. However, recent GWA studies and new high-throughput DNA sequencing techniques have provided new promise. Although there are good standards and practices to analyze GWAS data, the interpretation and analysis of sequence data are still in their infancy. This meeting brought together experts to critically assess current strategies and to outline how genome-scale sequencing can be used most effectively and efficiently. Topics covered included the following: How can high-throughput sequencing build on GWA studies? How should candidate rare risk alleles be validated? How will we ensure that data will be accessible to the community at large, while protecting the legitimate intellectual concerns of primary investigators, not to mention the privacy concerns of study subjects?

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

Introduction: W.R. McCombie, Cold Spring Harbor Laboratory
A. Palotie, University of Helsinki, Finland

SESSION 1: What Can We Learn from Genotype-Based Association Studies?

Chairperson: J. Knowles, University of Southern California, Los Angeles

P. Sullivan, University of North Carolina, Chapel Hill: PGC, update on the schizophrenia GWAS.

B. Neale, Harvard University, Boston, Massachusetts: Statistics, and why we need them.

T. Pers, Harvard University, Boston, Massachusetts: Selecting likely causal genes and pathways from GWAS by data integration.

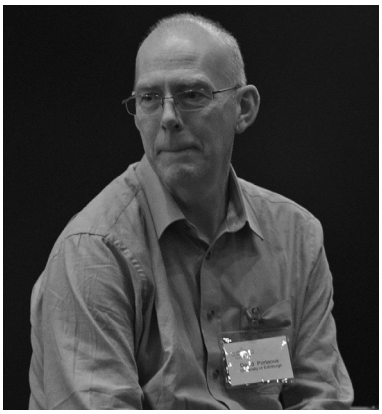
T. Lencz, North Shore LIJ Health System, Glen Oaks, New York: Genetic studies in schizophrenia: Expanding the scope by narrowing the focus.

General Discussion

SESSION 2: What Can We Learn from Sequence-Based Association Studies?

Chairperson: D. Porteous, University of Edinburgh, United Kingdom

S. Purcell, Mount Sinai School of Medicine, New York: Schizophrenia case control exome sequencing association.



D. Porteous

M. Daly, Harvard University, Boston, Massachusetts: Exome sequencing and the genetic architecture of autism spectrum disorders.

L. Scott, University of Michigan, Ann Arbor: Whole-genome and -exome sequencing of bipolar disorder.

D. Goldstein, Duke University, Durham, North Carolina: Lessons from Mendelian genetics in complex neuropsychiatric disease.

General Discussion

SESSION 3: What Can We Learn from Sequencing Families?

Chairperson: D. Goldstein, Duke University, Durham, North Carolina

J. Knowles, University of Southern California, Los Angeles: RNA-Seq: BrainSpan, CNON, and single cells.

D. Porteous, University of Edinburgh, United Kingdom: Generation Scotland GWAS for major depressive disorder and related traits.

A. Corvin, Trinity College, Dublin, Ireland: Common and rare variants implicate PAK signaling in psychosis susceptibility.

M. Wigler, Cold Spring Harbor Laboratory: Gene target discovery in autism by family exome sequencing.

M.-C. King, University of Washington, Seattle: Damaging de novo mutations in schizophrenia: Identification and mapping to prefrontal cortex.

J. McClellan, University of Washington, Seattle: Damaging de novo mutations in schizophrenia: Insights from gene function.

General Discussion

SESSION 4: What Can We Learn from More Detailed Analysis of the Phenotype and the Environment?

Chairperson: P. Sullivan, University of North Carolina, Chapel Hill

N. Freimer, University of California, Los Angeles: Genetics of brain and behavior: What is the right phenotype?

A. McIntosh, University of Edinburgh, United Kingdom: Quantification and stratification of depression for gene discovery.

M. Burmeister, University of Michigan, Ann Arbor: Gene *x* environment interactions play a role in human behavior and psychiatric disorders.

J. Smoller, Harvard Medical School, Boston, Massachusetts: DSM and beyond: Leveraging alternative phenotypic strategies.

General Discussion

SESSION 5: What Can We Learn from Using Alternative Approaches?

Chairperson: W.R. McCombie, Cold Spring Harbor Laboratory

A. Need, Imperial College, London, United Kingdom: Whole-genome sequencing in childhood psychiatric illness.

A. Palotie, University of Helsinki, Finland: Use of population isolates in disease genetics.

SESSION 6: How to Proceed to Understanding More About the Function

Chairperson: N. Freimer, University of California, Los Angeles

K. Brennand, Mount Sinai School of Medicine, New York: Validating genetic findings using human iPSCs.

W.R. McCombie, Cold Spring Harbor Laboratory: Heterogeneity and strategy: Ways to move to function.

Final Discussion: What Next?

Coffee break discussion

Accelerate Genomic Research with Privacy Protections

December 11–13

FUNDED BY **Illumina, Inc.**

ARRANGED BY **Y. Erlich,** Whitehead Institute, Cambridge, Massachusetts
R. Kain, Illumina, Inc., San Diego, California
A. Narayanan, Princeton University, New Jersey

In a decade, we have gone from sequencing megabases of DNA at great cost, to sequencing gigabases at low cost. Projects on a scale unimaginable a few years ago are now possible. The data from these projects, coupled with the healthcare records and other details of the life histories of the individuals, will be the foundation for a revolution in healthcare. One particular challenge is the personal privacy and the ultimate security of personal genome information. Even if the information is used in a de-identified manner for large-scale health studies, there is no guarantee that the information will not be traced back to the individual. There is a danger that the dialogue about the security of an individual's genome information will be driven by anecdotes and ill-considered reporting in scientific journals, the mainstream press, and social networks. We hope to minimize this risk by initiating a public discussion of these issues, recognizing the ethical and technical challenges of managing genomic information and suggesting possible solutions. To do so, we are bringing together scientists from the fields of human genetics, bioinformatics, cryptography, and privacy scholarship.

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

What the Meeting Is About: Y. Erlich, Whitehead Institute, Cambridge, Massachusetts

Introduction: Genomics and the Value of Data Dissemination
T. Manolio, National Human Genome Research Institute, Rockville, Maryland

SESSION 1: Anatomy of Hacks: Vulnerability Points and Areas of Vulnerability

Chairperson: R. Kain, Illumina, Inc., San Diego, California

B. Malin, Vanderbilt University, Nashville, Tennessee: Genomics and the wonderful world of re-identification.

Y. Erlich, Whitehead Institute, Cambridge, Massachusetts: Identifying personal genomics by surname inference.

General Discussion

SESSION 2: Current State of Ecosystem: Summary of Ethical and Policy Considerations

Chairperson: R. Kain, Illumina, Inc., San Diego, California

N. Farahany, Duke University, Durham, North Carolina: US and EU privacy frameworks for genomics.

SESSION 3: Approaches to Risk Analysis: Future Vulnerability and Impact

Chairperson: R. Kain, Illumina, Inc., San Diego, California

S. Brenner, University of California, Berkeley: Premises in genome privacy.

D. Glazer, Google, Mountain View, California: Google's privacy principles.

General Discussion

SESSION 4: The Sandbox Model and Access Control

Chairperson: Y. Erlich, Whitehead Institute, Cambridge, Massachusetts

S. Sherry, National Library of Medicine, Bethesda, Maryland: An overview of DBGap, content, format, and access.

R. Shelton, Private Access, Inc., Irvine, California: Consumer-controlled empowered tools for harmonizing privacy and access to confidential information.

A. Philippakis, Broad Institute, Boston, Massachusetts: Genome Bridge, a cloud-based platform for genome-scale analysis: How it works, how is privacy managed.

General Discussion

SESSION 5: Differential Privacy: Quantitative Methods for Data Perturbation or Restricting Queries to Ensure Privacy

Chairperson: Y. Erlich, Whitehead Institute, Cambridge, Massachusetts

A. Narayanan, Princeton University, New Jersey: Introduction and framing: Cryptography and differential privacy (why it's included).

V. Shmatikov, University of Texas, Austin: Attempting to apply differential privacy to genome-wide association studies.

General Discussion

SESSION 6: Cryptographic Approaches for Data Dissemination

Chairperson: Y. Erlich, Whitehead Institute, Cambridge, Massachusetts

E. Eskin, University of California, Los Angeles: Identifying genetic relatives without compromising privacy.

J. Witkowski, S. Turner, M. Olson, T. Hunkapiller

R. Shelton, Y. Erlich, and T. Manolio list topics for discussion

G. Tsudik, University of California, Irvine: How medical predictions can be made from DNA data using homomorphic encryption.

General Discussion

SESSION 7: Interdependencies: Technology Solutions vs. Ethics and Public Policy/Legislation

Chairperson: A. Narayanan, Princeton University, New Jersey

T. Callaghan, Federal Bureau of Investigation, Quantico, Virginia: Law enforcement databases: Tensions between forensic analysis and genetic privacy.

C. Ball, Ancestry DNA, San Francisco, California: DTC testing and the consumer's attitude toward genetic privacy.

L. Rodriguez, National Human Genome Research Institute, Bethesda, Maryland: Moving forward: Evolving policy considerations regarding genomic privacy.

General Discussion

SESSION 8: Summaries and Proposed Outcomes

White paper: Which five key points to include?

Summary and Concluding Remarks

L. Stein, C. Ball

Phelan-McDermid Syndrome: Autism due to Shank3 Mutations/Deletions

December 15–17

FUNDED BY **Phelan-McDermid Syndrome Foundation**

ARRANGED BY **G. Bliss,** Phelan-McDermid Syndrome Foundation, Houston, Texas
R. Dolmetsch, Allen Brain Institute, Stanford, California
C. Powell, University of Texas Southwestern, Dallas

The goals of this discussion meeting were to share the most current research on Shank3-related neurodevelopmental disorders and to design a plan for near-term and long-term research aimed at understanding and treating Shank3-related symptoms. A carefully selected group of scientists and clinicians from diverse backgrounds and interests discussed their most recent data and their candid thoughts on the most promising future avenues of research. Participants shared unpublished data, future research plans, and constructive criticism of published data in the field. Discussion sessions with appointed leaders were interleaved among the talks to encourage goal-directed brainstorming that was hoped would lead to clear future objectives. It was expected that at the conclusion of the meeting, participants would come away with a clear picture of the challenges that lie ahead and strategies to overcome them.

K. Phelan

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

SESSION 1: Toward a Natural History of PMS

G. Bliss, Phelan-McDermid Syndrome Foundation, Houston, Texas: Registry.
C. Betancur, INSERM-CNRS, Paris, France: Clinical genetics.
K. Phelan, Tulane University School of Medicine, New Orleans, Louisiana: PMS in adolescents and adults.
A. Kolevzon, Icahn School of Medicine at Mt. Sinai, New York: Natural history.

Session Discussion: How to Proceed to Obtaining Information about Natural History?
Moderator: A. Hardan, Stanford University, California

SESSION 2: Toward Clinical Trial Design in PMS

J. Buxbaum and A. Kolevzon, Icahn School of Medicine at Mt. Sinai, New York: PMS clinical trial: Rationale, design, outcome measures.
J. Neul, Baylor College of Medicine, Houston, Texas: Rett syndrome clinical trial outcome measures.
R. Carpenter, Seaside Therapeutics, Cambridge, Massachusetts, and M. Bear, Massachusetts Institute of Technology: Fragile X clinical trial outcome measures.
M. Sahin, Children's Hospital, Boston, Massachusetts: TSC clinical trial outcome measures; Mechanisms of neurocognitive dysfunction and treatment trials in TSC.

Session Discussion: How to Discover and Define Most Appropriate Outcome Measures for Clinical Trials in PMS?
Moderator: J. Veenstra-Vanderweele, Vanderbilt University, Nashville, Tennessee

SESSION 3: Therapeutic Target Identification for PMS in Model Systems: Study, Replicate, Repeat

R. Dolmetsch, Novartis Institute for BioMedical Research, Inc., Cambridge, Massachusetts: Human neuronal cultures.

C. Powell, G. Bliss

R. Dolmetsch

C. Sala, CNR: Institute of Neuroscience, Milan, Italy: Animal neuronal cultures.
Z. Yan, State University of New York, Buffalo: Shank3 deficiency causes synaptic and behavioral impairment via an actin-dependent mechanism.

Session Discussion: In Vitro Models: How Best to Use Them?
Moderator: W. Spooren, F. Hoffmann-LaRoche Ltd., Basel, Switzerland
Do the cultures and animal models overlap?
How can we move rationally to high-throughput screening that is meaningful?
Consensus on how targets should be preclinically validated?

SESSION 3 (continued): Therapeutic Target Identification for PMS in Model Systems

J. Buxbaum, Icahn School of Medicine at Mt. Sinai, New York: Animal models 1: Exon 4–9 (Ankryin repeat domain).
C. Powell, University of Texas, Dallas: Animal models 3: Exon 21 (Homer-binding domain).
Y.-H. Jiang, Duke Institute for Brain Sciences, Durham, North Carolina: Animal models 4: Complete deletion.
J. Holder, Baylor College of Medicine, Houston, Texas: Animal models 5: SHANK3 overexpression; Overexpression of Shank3 causes a unique neuropsychiatric disorder.

Session Discussion: Animal Models: How Best to Use Them?
Moderator: T. Boeckers, Universität Ulm, Germany
What replicates, what does not, why?
What convergence is there if any?
What brain regions are most critical?
What treatments should be studied next in the models?
What are the key issues for future research?

SESSION 4: Goal-Directed Group Discussion

D. Bredt, Johnson & Johnson Pharmaceutical R&D, San Diego, California: Preclinical studies.
W. Kaufmann, Boston Children's Hospital, Massachusetts: Clinical studies and outcome measures.
C. Powell, University of Texas, Dallas: Therapeutic targets and screening.
W. Spooren, F. Hoffmann-LaRoche Ltd., Basel, Switzerland: EU-AIMS.

Final Discussion: What Are the Key Issues, What to Do Next?

- Toward a natural history of PMS
- Toward clinical trial design in PMS
- Therapeutic target identification for PMS in model systems
- Funding
- Dissemination

BANBURY CENTER GRANTS

Grantor	*Program*	*Duration of Grant*	*2013 Funding*
FEDERAL SUPPORT			
National Institute on Alcohol Abuse and Alcoholism	The Adolescent Brain	2013	$ 4,635
National Institute of Mental Health	The Adolescent Brain	2013	4,635
NONFEDERAL SUPPORT			
Allen Institute for Brain Science	The Adolescent Brain	2013	10,500
ALS Association of Greater New York	Development and Evolution of the Human Motor System in Relation to ALS and FTD	2013	46,367
Boehringer Ingelheim Fonds	Science: Get It Across!	2013	58,594
John K. Castle	Oxidants and Antioxidants in Cancer Genesis and Treatment	2013	20,000
Cold Spring Harbor Laboratory Corporate Sponsor Program	Evolution of Plant Metabolic Diversity	2013	43,732
	Redesigning Photosynthesis: Identifying Opportunities and Novel Ideas	2013	58,988
	Telomeres and Disease	2013	48,358
Cold Spring Harbor Laboratory–DuPont Pioneer Collaborative Research Program	Plant Reproduction	2013	50,000
Dart NeuroScience	Transposable Elements in the Brain and Other Tissues: Prevalence and Function	2013	19,053
Illumina, Inc.	Accelerating Genomic Research with Privacy Protections	2013	34,410
Individual participants	The Adolescent Brain	2013	6,090
Individual participants	Developing a Neuroscience Consortium	2013	23,270
Individual participants	The Emerging Intersection between the Physical Sciences and Oncology	2013	2,060
Individual participants	Grand Challenges in Organismal Biology	2013	1,375
Individual participants	The Neurobiology and Clinical Study of Rapid-Acting Antidepressants	2013	5,500
ISCTM	Developing a Neuroscience Consortium	2013	7,495
Janssen Research & Development	The Neurobiology and Clinical Study of Rapid-Acting Antidepressants	2013	34,362
Kotumba Capital Management, LLC	Science of Pancreatic Cancer	2013	12,572
The Lieber Institute for Brain Development	The Adolescent Brain	2013	12,500
Elizabeth Livingston Estate	Interdisciplinary Approaches to Idiopathic Lung Fibrosis	2013	43,648
Lustgarten Foundation	Lustgarten Foundation Annual Scientific Meeting	2013	38,764
MCJ Amelior Foundation	Science of Pancreatic Cancer	2013	20,060
Oliver Grace Cancer Fund	Oxidants and Antioxidants in Cancer Genesis and Treatment	2013	41,233
Oliver Grace Cancer Fund	Biguanides and Neoplasia	2013	59,632
Oliver Grace Cancer Fund	Enhancer Biology in Health and Disease	2013	51,718
Ovarian Cancer Research Fund	Ovarian Cancer: Developing Research-Based Public Messaging on Early Detection and Screening	2013	31,544
Pfizer, Inc.	INK4a/ARF Network	2013	56,000
Phelan McDermid Syndrome	Autism due to Shank3 Mutations/Deletions Foundation	2013	33,121
Marie Robertson Neuroscience Fund	Transposable Elements in the Brain and Other Tissues: Prevalence and Function	2013	20,000
The Daniel & Joanna S. Rose Foundation	Consciousness and the Brain	2013	10,000

BANBURY CENTER GRANTS (*Continued*)

Grantor	*Program*	*Duration of Grant*	*2013 Funding*
The Satenik and Adom Ourian Educational Foundation	Consciousness and the Brain	2013	$ 1,000
Stanley Research Foundation	Psychiatric Genomics: Current Status, Future Strategies	2013	41,335
Stony Brook University through a grant from NSF	Grand Challenges in Organismal Biology	2013	42,625
University of Southern California NCI Physical Sciences in Oncology Center	The Emerging Intersection between the Physical Sciences and Oncology	2013	27,372

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