# CSH Cold Spring Harbor Laboratory 2015 BANBURY CENTER

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# 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: A fall day at the Banbury Center.

Mailing address: Banbury Center, Cold Spring Harbor Laboratory, P.O. Box 534, Cold Spring Harbor, New York 11724 Street address: Banbury Center, Banbury Lane, Lloyd Harbor, New York 11743 Telephone: (516) 367-8398 Fax: (516) 367-5106 E-mail: banbury@cshl.edu Internet: http://www.cshl.edu/banbury BANBURY CENTER EXECUTIVE DIRECTOR'S REPORT

It was in June 1975 that the Cold Spring Harbor Laboratory Board of Trustees passed a motion accepting "...enthusiastically and with gratitude" Charles Robertson's gift of his estate. The official opening was in May 1977 when Francis Crick gave a talk on "How Scientists Work," and the first meeting was held in April 1978. The Center has been extraordinarily successful, fulfilling Robertson's visions of contributing to science through promoting exchanges of information and ideas. Since 1978, Banbury has held more than 650 meetings attended by more than 13,000 participants coming from 40 countries and every state in the United States with one exception-Alaska. These raw numbers do not convey the influence that Banbury meetings have had, and continue to have, in the development of biomedical research. This influence is felt not only in research but also in areas of science policy. Charles Robertson, I hope, would feel that his gift has been well used.



Charles and Marie Robertson, late 1960s

# Funding of the Banbury Center Program

As a preamble to the 2015 report, I want to make some remarks about changes in the Banbury Center program over the years, changes driven primarily by changes in funding. For many years, the generous contributions of companies to the Cold Spring Harbor Laboratory Corporate Sponsor Program (CSP) were a source of stable funding both for the Banbury Center program and for supporting meetings on the main campus. The CSP funds were particularly valuable because



Robertson House, 1934



Conference Room

although they were restricted to the support of meetings, they were not restricted to the funding of meetings on specific topics. The choice of which meetings should be supported by Corporate Sponsor Program funds was left to the directors of the two programs.

The Banbury allocation of the CSP funds was invaluable. First, the funds provided support for about one-third of the Banbury program, thus providing a firm foundation for the Center. Second, the CSP funds could be and were used to fund meetings on basic research for which support would otherwise have been difficult to find. This enabled the Center to have meetings on a wide variety of topics.

Membership in the CSP dwindled as the large number of mergers in the pharmaceutical and biotechnology industries reduced the pool of potential members and declined precipitously following the recession. Although matters have improved, several major companies who left in the period 2008–2012 have not returned and the Program remains severely depleted. The consequences of this are visible in the 2015 program, where meetings on cancer and relating to the brain dominate because funding is relatively more available for these topics. Jim Watson and Hakon Heimer have been particularly helpful in finding funds for the former and latter meetings, respectively. And, of course, we are tremendously grateful to our current Corporate Sponsors for their continuing support.

# 2015 in Numbers

Despite the continuing funding difficulties, the 2015 program proved to be a busy one. The Conference Room was used for 37 events, including 21 Banbury Center meetings. There were 621



Robertson House cocktails

participants at these meetings, drawn from 35 states with California, Maryland, Massachusetts, and New York leading the way. The proportion of non-U.S. participants was a little lower this year at 16%, coming from 17 countries. Thirty percent of participants were female. As usual, there were summer lecture courses and the Watson School of Biological Sciences came for two week-long courses. In 2015, a strategic alliance was established between CSHL and the then North Shore–Long Island Jewish healthcare system (now Northwell Health) to promote scientific and clinical research on cancer. The Center is being used for joint meetings between researchers and oncologists, helping to promote collaborations between the two institutions.

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# **HIV/AIDS**

Although the Banbury Center has a long history of meetings on HIV/AIDS, the 2015 meeting HIV-1 and How to Kill a Killer: Attempts at Total or Functional Cure of HIV-1 was the first meeting on HIV/AIDS in 26 years. The first meeting was in 1983 when William Topp (CSHL) and Bijan Safai (Memorial Sloan Kettering Cancer Center, New York) organized Acquired Immunodeficiency Syndrome (AIDS) and Human Immunodeficiency Virus (HIV). By 1988, it was known that HIV was the causative agent, but the virus was complex and its interactions with the host cell were hard to unravel. The Banbury meetings in 1988 and 1989 on the Control of HIV Gene Expression dealt with these questions: What were the HIV genes and what did they do in the cell? Perhaps it was thought that the plethora of AIDS/HIV meetings in subsequent years made superfluous Banbury meetings on the topic, but a new development led to the 2015 meeting. In 2014 two children given antiretroviral therapy and believed to be HIV-free relapsed when the therapy stopped. The question this raised was where might the virus have been hiding? The organizers, Robert Gallo (University of Maryland, Baltimore), Steven Deeks (University of California, San Francisco), and Robert Siliciano (Johns Hopkins University, Baltimore, Maryland) and the participants reviewed topics such as the mechanism of HIV latency, how to better assay HIV, and what leads to the reversal of HIV latency.

# **Neurodegenerative Disorders**

Neurodegenerative disorders characterized by protein misfolding have long been a focus of Banbury Center meetings. The first meeting on Alzheimer's disease was held in 1982, and 33 years later, we continued to review the research on the basic mechanism of abnormal protein folding and aggregation in *Biophysical Properties and Biological Significance of Amyloid-\beta Assemblies.* 

Stanley Prusiner, who won the Nobel Prize for Physiology or Medicine, contributed a paper on prions to the 1982 meeting and subsequently organized a meeting on prions, the first of a series, the latest of which, *Therapeutic Approaches to Prion Disease and Other Neurodegenerative Conditions*, was held in 2015. It was interesting to see how the field has progressed from studies on the nature and mechanism of prion formation through to enabling discussion of possible therapies.

# **Psychiatric Disorders**

This general field continues to be a mainstay of the Banbury program, and through the work of Hakon Heimer, we were able to hold four meetings this year focused on therapeutic approaches to relieving the distress of mental illness. *Therapeutic Use of Ketamine for Treating Severe Depression: Risks and Potential* followed up on a meeting on ketamine and depression held in 2012. That meeting reviewed what is known of ketamine's mode of action and its effectiveness in relieving profound depression. The 2015 meeting examined the impediments to the use of ketamine for treating depression. It was a very effective meeting, and it may lead to new treatment recommendations.

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Deep brain stimulation (DBS) has been used successfully to treat people with severe mental illness, although it is not clear exactly how it brings benefit to patients. However, DBS requires implantation of electrodes in the brain—surgery that severely limits the application of DBS. Participants in *Brain Rhythms as Potential Targets for Intervention in Cognitive Dysfunctions* reviewed the current state of methods to stimulate the brain noninvasively, electrically or magnetically. In addition to scientific and clinical considerations involved, the meeting closed with a session discussing the ethical and regulatory issues.

Schizophrenia is a devastating disorder, both for the individual and for the family. The lives of many people with schizophrenia could be radically improved if they had full access to proven treatments and support services. These include pharmacologic therapy, cognitive training, and environmental support. However, it has been difficult to identify which treatments are effective and which can be widely deployed. This is especially difficult because of considerable variation in individual responses—one individual may experience relief by a treatment that is ineffective in others. Participants in *Thriving with Schizophrenia* evaluated the research base underlying treatment/support methods and identified those that are promising but require further research.

The fourth of the meetings was on the genetics and neurobiology of borderline personality disorder (BPD), a disabling condition with high morbidity and substantial mortality. Indeed, 10% of people with BPD die by suicide, and BPD is a risk factor for treatment-refractory depression. A high proportion of psychiatrically hospitalized patients carry the diagnosis of BPD, and even the best available treatment typically does not attenuate all of the symptoms of BPD, even in those who respond well to treatment. Although neglected for many years, research is revealing that it is a highly heritable disorder with associated functional abnormalities in brain circuitry. Nevertheless, an understanding of its pathophysiology remains elusive. The aim of this conference was to draw attention to the neurobiological research in BPD and to bring together individuals from a variety of disciplines to drive forward scientific knowledge that will advance treatment for this disorder.

### Cancer

Although studies of the genetics and genomics of cancer continue apace, there has been a significant increase in research on the metabolic changes in cancer cells. This is of particular interest to Jim Watson, whose Oliver Grace Cancer Fund provided support for two meetings in this field. The first, *Mitochondria and Cancer*, was organized by Navdeep Chandel (Northwestern University, Chicago, Illinois) and David Sabatini (Whitehead Institute, Cambridge, Massachusetts) and reviewed what is known in the field. Although the majority of cancer cells display functional mitochondria, there are small subsets of cancer cells with impaired mitochondrial function. These cells can nevertheless perform biosynthetic functions for macromolecule synthesis. Overall, the accumulating evidence now suggests that mitochondrial bioenergetics, biosynthesis,



Redtail hawk

and signaling are required for tumorigenesis. One goal of the meeting was to identify possible targets of mitochondrial metabolism for cancer therapy.

The second meeting had a similar goal but considered the problem more broadly. *Tumor Cell Metabolism: Finding New Targets for Therapeutic Intervention* was organized by Lewis Cantley (Weill Cornell Medical College, New York) and Steven McKnight (University of Texas Southwestern Medical Center, Dallas). Participants reviewed new metabolic targets, discussed biomarkers which may predict which tumors are likely to respond to drugs that hit these targets, examined potential

mechanisms of resistance to such therapies, and discussed drug combinations that could prevent resistance.

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# **Promoting Research**

Banbury takes special pride in meetings that have contributed to research by helping organizations and foundations plan future research or by training the next generation of scientists. The Boehringer Ingelheim Fonds once again came to Banbury for their Fellows Retreat, in which the fellows are given training in writing and giving talks. This is the 10th year that the Foundation has brought its fellows to Banbury and we hope very much that we will continue to help the Foundation fulfill its goal of training the next generation of scientists.

Banbury also hosted a meeting that was designed to help a new foundation develop its plan of action. The Foundation is HeritX and the goals of the meeting were succinctly encapsulated in its title: *Preventing Inherited BRCA Cancer: A Think Tank for Innovative Strategies, Milestone Objectives, and Research Priorities.* Over two days of intensive review and discussion, HeritX developed a road map for its future.

## Acknowledgments

Banbury works well because of the hard work of many people, not least Janice Tozzo and Pat Iannotti in the Banbury Center office. Now, after 7 years of ensuring that I completed tasks on time and did not forget meetings, Janice has retired to concentrate on her glass sculptures and Michelle Corbeaux has come to take her place. Basia Polakowski continues to welcome and look after participants in Robertson House, and Jose Covera, Joe McCoy, and Saul Covera keep the estate looking beautiful, coping with huge quantities of leaves in the fall and snow in the winter. Culinary Services, Facilities, and the Meetings Office play key roles in the operation of the Center. The meetings would not be the success they are without the contributions of organizers and participants, the generosity of the Laboratory's Corporate Sponsors and the other donors who fund our meetings, and the Laboratory's scientists who continue to support the Center.

> Jan A. Witkowski Executive Director

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# **BANBURY CENTER MEETINGS**

Date	Title	Organizer(s)
February 20–25	Communicating Science	C. Walther, S. Schedler
March 9–11	Exercise Science and Health	R. Pate, T. Church, L. Goodyear
March 17–20	Brain Rhythms as Potential Targets for Intervention in Cognitive Dysfunctions	M. Garvey, B. Osborn, R. Cohen Kadosh, B. Postle
April 6–9	Biophysical Properties and Biological Significance of Amyloid-β Assemblies	K. Ashe, R. Tycko
April 14–17	Creating Patient-Specific Neural Cells for the In Vitro Study of Brain Disorders	F. Gage, R. Jaenisch
April 19–22	Neuronal Response Variability and Correlation	L. Abbott, K. Rajan, J. Reynolds
April 25–27	Beyond the Wheat Genome	M. Caccamo
May 1–3	NIMH Brain Camp VII	T. Insel, J. Chung
June 14–17	Thriving with Schizophrenia	L. Dixon, H. Heimer, J. Kane, M. Munetz, R. Heinssen
June 18–20	Integrated Translational Science Center Workshop	L. Baker, L. Ellis, E. Liu, A. Schott, D. Tuveson
September 1-4	Mitochondria and Cancer	N. Chandel, D. Sabatini
September 15–18	Therapeutic Approaches to Prion Disease and Other Neurodegenerative Conditions Associated with Protein Misfolding	J. Collinge, J. Kelly
September 20-22	Therapeutic Use of Ketamine for Treating Severe Depression: Risks and Potential	R. Robinson Beale, H. Heimer, J.A. Witkowski
September 27–30	Therapeutic Developments for ALS: Antisense, Gene Therapy, and Stem Cells	L. Bruijn, T. Miller, C. Svendsen, D. Sah
October 4–7	What Is Needed to Harness Chemogenetics for the Treatment of Human Brain Disorders?	G. Aston-Jones, T. Kash
October 13-16	HIV-1 and How to Kill a Killer: Attempts at Total or Functional Cure of HIV-1	R. Gallo, S. Deeks, R. Siliciano
October 18-20	The Lustgarten Foundation Scientific Meeting	C. Ardito-Abraham, D. Tuveson
November 1–4	Scientific and Clinical Foundation for Precision Medicine in Epilepsy	S. Berkovic, E. Heinzen Cox, D. Goldstein, D. Lowenstein
November 11–13	Preventing Inherited BRCA Cancer: A Think Tank for Innovative Strategies, Milestone Objectives, and Research Priorities	A. Ashworth, T. Bock, L. Brody
November 15–18	How Can the Genetics and Neurobiology of Borderline Personality Disorder Contribute to Its Diagnosis and Treatment?	J. Oldham, A. New
December 7–10	Tumor Cell Metabolism: Finding New Targets for Therapeutic Intervention	L. Cantley, S. McKnight

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# BANBURY CENTER MEETINGS

# **Communicating Science**

# February 20-25

FUNDED BY	Boehringer Ingelheim Fonds Foundation for Basic Research in Medicine
ARRANGED BY	C. Walther, Boehringer Ingelheim Fonds, Mainz, Germany S. Schedler, Boehringer Ingelheim Fonds, Mainz, Germany

The Boehringer Ingelheim Fonds' international program of support for Ph.D. fellowships 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 2015 stay at Banbury was the eighth occasion that 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.

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

Opening Remarks and All About BIF-Part 1: C. Walther, Boehringer Ingelheim Foundation, Mainz, Germany

Communication-Why and How ?: K. Achenbach, Boehringer Ingelheim Foundation, Mainz, Germany

N. LeBrasseur, DNA Medical Communications, New York: Writing techniques and how to structure papers: Writing assignment 1. B. Tansey, Vanderbilt University, Nashville, Tennessee: Preparing and delivering a scientific talk.



The Boehringer Ingelheim fellows in the Meier House

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- Group A: 4-min PowerPoint presentations, videotaped with replay and feedback.
- N. LeBrasseur, DNA Medical Communications, New York: Discussion of writing assignment 1: Writing assignment 2.
- B. Tansey, Vanderbilt University, Nashville, Tennessee: Power-Point presentations.
- N. LeBrasseur, DNA Medical Communications, New York: Return and discussion of writing assignment 2.
- B. Tansey, Vanderbilt University, Nashville, Tennessee: Group B: 3-min PowerPoint presentations, videotaped with replay and feedback.

- M. Skobe, Mount Sinai School of Medicine: Career talk.
- K. Ris-Vicari, Katie Ris-Vicari Graphic Design, Bethpage, New York, and
- M. Hansen, Nature Publishing Group, New York: How to design figures.
- All About BIF—Part 2 and Feedback: C. Walther, Boehringer Ingelheim Foundation, Mainz, Germany

Guided Walking Tour on CSHL Campus

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# **Exercise Science and Health**

# March 9-11

FUNDED BY	Oliver Grace Fund
ARRANGED BY	<ul> <li>R. Pate, University of South Carolina, Columbia</li> <li>T. Church, Pennington Biomedical Research Center, Baton Rouge, Louisiana</li> <li>L. Goodyear, Joslin Diabetes Center and Harvard Medical School, Cambridge, Massachusetts</li> </ul>

Exercise is regarded as a key component of healthy living, and yet there appears to be little consensus on how exercise regimens can be used most efficiently and optimized for promoting health. Participants in this meeting considered several questions on health and exercise, including the following: What conditions benefit from exercise? What mediates the beneficial effects of exercise? What exercise regimens are effective? What, if any, are the interactions between exercise and nutrition? Can understanding the pathways by which exercise brings about its effects be useful in guiding the development of drugs?

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

Introduction: R. Pate, University of South Carolina, Columbia

SESSION 1: Type-2 Diabetes and the Metabolic Syndrome

- Chairperson: W. Kraus, Duke University Medical Center, Durham, North Carolina
- J. Wojtaszewski, University of Copenhagen, Denmark: Mechanisms in exercise-induced muscle insulin sensitivity.
- B. Goodpaster, Sanford–Burnham Medical Research Institute, Orlando, Florida: The impact of exercise on type-2 diabetes and cardiometabolic risk.
- A. Kriska, University of Pittsburgh, Pennsylvania: Impact of the successful diabetes prevention program's lifestyle intervention. What progress has been made in efforts to translate this knowledge to the public health arena?

# **General Discussion**

### **POSTER SESSION**

### SESSION 2: Healthy Aging

- Chairperson: R. Fielding, Tufts University, Boston, Massachusetts
- A. Wagers, Harvard University, Cambridge, Massachusetts: Local and systemic regulators of aging phenotypes in mammalian tissue.
- T. Church, Pennington Biomedical Research Center, Baton Rouge, Louisiana: Exercise and quality of life: The forgotten benefit.

D. Buchner, University of Illinois, Champaign: Public health strategies for promoting physical activity and healthy aging.

SESSION 3: Muscle Hypertrophy and Sarcopenia

- Chairperson: B. Goodpaster, Sanford–Burnham Medical Research Institute, Orlando
- T. Hornberger, University of Wisconsin, Madison: The potential role of lysosomal targeting in the mechanical activation of mTOR.
- R. Fielding, Tufts University, Boston, Massachusetts: Muscle hypertrophy and sarcopenia: Clinical science.

### **General Discussion**

#### SESSION 4: Selected Presentations

- Chairperson: B, Goodpaster, Sanford–Burnham Medical Research Institute, Orlando, Florida
- J. Mitchell, University of Pennsylvania, Philadelphia: The benefits of physical activity on bone density in childhood are dependent on genetic variation at known bone density loci.
- J. Valentine, University of Texas Health Science Center, San Antonio: Inhibition of NF-κB causes muscle weakness and severe exercise intolerance.

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X. Wang, University of South Carolina, Columbia: Changes in nonexercise activity thermogenesis with participation in exercise training in older women: Preliminary results from the WeWalk study.

### SESSION 5: Physical Activity and Cognition

- Chairperson: J. Pivarnik, Michigan State University, East Lansing
- M. Voss, University of Iowa, Iowa City: Effects of exercise on functional brain networks and cognitive performance in aging adults.
- J. Reilly, University of Strathclyde, Glasgow, United Kingdom: Physical activity and cognition: Clinical science.
- R. Pate, University of South Carolina, Columbia: Physical activity and children's learning: Ready for public health prime time?

#### **General Discussion**

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- SESSION 6: Parental Exercise/Exercise during Pregnancy and Child Health
- Chairperson: J. Reilly, University of Strathclyde, Glasgow, United Kingdom
- L. Goodyear, Joslin Diabetes Center and Harvard Medical School, Cambridge, Massachusetts: Effects of maternal exercise on metabolic health of offspring.

- J. Pivarnik, Michigan State University, East Lansing: Exercise during pregnancy: Where we have been, where we are going? L. Chasan-Taber, University of Massachusetts, Amherst:
- Exercise interventions in high-risk pregnant and postpartum women: Opportunities and challenges.
- SESSION 7: Exercise Resistance: Genetic Nonresponse and Compliance with Exercise

Chairperson: D. Buchner, University of Illinois, Champaign

- C. Bouchard, Pennington Biomedical Research Center, Baton Rouge, Louisiana: Poor response of cardiorespiratory fitness with exposure to regular exercise: Evidence for a genetic basis.
- B. Kraus, Duke University Medical Center, Durham, North Carolina: Molecular predictors of exercise nonresponsiveness and program adherence.
- R. Dishman, University of Georgia, Athens: Exercise adherence and compliance: Motivation and genes.

SESSION 8: Concluding Discussion: Health and Exercise

- Moderator: L. Goodyear, Joslin Diabetes Center and Harvard Medical School, Cambridge, Massachusetts
- Are all patterns of exercise equally effective in promoting health?
- How little exercise is needed to achieve a benefit?
- What can be done for public health?



L. Chasan-Taber

L. Xing, W. Song



W. Kraus

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# Brain Rhythms as Potential Targets for Intervention in Cognitive Dysfunctions

# March 17-20

funded by	National Institute of Mental Health, National Institutes of Health
ARRANGED BY	M. Garvey, National Institute of Mental Health, Rockville, Maryland B. Osborn, National Institute of Mental Health, Rockville, Maryland R. Cohen Kadosh, University of Oxford, United Kingdom B. Postle, University of Wisconsin, Madison

Optimal cognitive and emotional processing arises from the simultaneous and successive interplay of large ensembles of neurons in multiple brain regions. One organizing principle appears to be the temporal dynamics of systems-level neural activity, such as electrophysiologically recorded oscillations, including their coordination across frequency bands and with action potentials. The goals of this Banbury meeting included examining current knowledge about how systems-level temporal dynamics supports cognitive and emotional processing and how this might be used to enhance cognitive and emotional processing.

There is also the potential to improve functional outcomes in patients with neuropsychiatric disorders. In addition, participants looked more broadly at the ethical and regulatory considerations for electrophysiological treatments.

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

Goals and Vision for the Meeting: B. Osborn, National Institute of Mental Health, Rockville, Maryland

**SESSION 1:** Temporal Dynamics for Therapeutic Use

T. Buschman, Princeton University, New Jersey: Dynamic synchronous ensembles for creating flexible task representations.





- B. Pesaran, New York University, New York: Controlling computations in large-scale neural circuits: Today and tomorrow.
- B. Postle, University of Wisconsin, Madison: Concurrent TMS unmasks functionally relevant endogenous components of task-related EEG.
- G. Thut, University of Glasgow, Scotland: Modulating brain oscillations by transcranial brain stimulation to drive brain function.
- J. Voss, Northwestern University, Chicago, Illinois: Altering hippocampal-cortical networks and memory using noninvasive stimulation.
- C. Herrmann, Oldenburg University, Germany: Modulating brain oscillations and cognitive functions with transcranial alternating current stimulation (tACS).
- Y. Saalmann, University of Wisconsin, Madison: Thalamocortical dynamics in cognition.
- B. Voytek, University of California, San Diego: Dynamic network communication as a unifying neural basis for cognition, development, aging, and disease.
- D. Tucker, University of Oregon, Eugene: Spatial and temporal resolution of geodesic transcranial electrical neuromodulation.
- V. Sohal, University of California, San Francisco: Rescuing PFC-dependent cognition by restoring interneuron-driven gamma oscillations.
- F. Frohlich, University of North Carolina, Chapel Hill: Rational design of brain stimulation that targets oscillation dynamics.
- A. Fenton, New York University, New York: The microstructure of cognition-associated neural coordination can distinguish between cognitive states and identify dysfunction.

### **General Discussion**

### SESSION 2: Clinical Implications

Chairperson: A. Pascual-Leone, Harvard Medical School, Boston, Massachusetts

- E. Berry-Kravis, Rush University Medical Center, Chicago, Illinois: Excitation-inhibition coordination.
- A. Benasich, Rutgers University, Newark, New Jersey: Defining the functional role of cortical oscillatory dynamics across

maturation and identifying potential biomarkers as targets for noninvasive behavioral interventions.

- A. Wheeler, RTI International, Research Triangle Park, North Carolina: Logistical challenges and potential solutions for measuring brain rhythms in individuals with neurodevelopment and neuropsychiatric disorders.
- S. Molholm, Albert Einstein College of Medicine, Bronx, New York: Sensorimotor networks and multisensory networks. In autism as well as other DDs, these domains are clearly impacted and have implications for the clinical phenotype.
- S. Loo, University of California, Los Angeles: Using cognitive deficits to identify brain oscillatory targets in neurodevelopmental disorders.
- R. Cohen Kadosh, University of Oxford, United Kingdom: Improving learning outcomes in participants with typical and atypical development using transcranial random noise stimulation.

### **General Discussion**

SESSION 3: Ethical and Regulatory Considerations

Chairperson: B. Postle, University of Wisconsin, Madison

- M. Barilan, Tel Aviv University, Israel: Moral enhancement: Is it enhancement? Is it moral?
- P. Reiner, University of British Columbia, Vancouver, Canada: Neuroethics of optimizing brain rhythms.
- E. Civillico, Food and Drug Administration, Silver Springs, Maryland: Regulatory science and brain oscillations.
- A. Pascual-Leone, Harvard Medical School, Boston, Massachusetts: Report from the Institute of Medicine meeting.
- M. Garvey, National Institute of Mental Health, Rockville, Maryland: Translational and clinical steps forward.

### **SESSION 4:** Future Directions

- Chairperson: B. Postle, University of Wisconsin, Madison: Where are we now?
- Gap areas and opportunities.
- Setting the agenda for future research.
- Documenting meeting outcomes.



A. Fenton

Y. Barilan



E. Berry-Kravis

# Biophysical Properties and Biological Significance of Amyloid-β Assemblies

## April 6-9

funded by	The Grossman Center of the University of Minnesota; Eli Lilly and Company; and Kyowa Hakko Kirin Co., Ltd.
ARRANGED BY	K. Ashe, University of Minnesota Medical School, Minneapolis R. Tycko, National Institute of Diabetes, Digestive, and Kidney Disease, Bethesda, Maryland

There is general agreement that self-assembly of the amyloid- $\beta$  (A $\beta$ ) peptide in brain tissue leads to neurodegeneration in Alzheimer's disease (AD), and it is also clear that many different selfassembled states exist both in vitro and in vivo. However, there is no consensus on which of these self-assembled states has the most significant role in AD development and how these lead to neurodegeneration. Participants critically reviewed what is currently known of the molecular structures of A $\beta$  fibrils and oligomers, the biological effects of self-assembled A $\beta$ , methods for detecting A $\beta$  assemblies in human and transgenic animal brain tissue, and approaches to inhibiting clinically significant A $\beta$  assemblies.

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

Opening Remarks and Overviews: K. Ashe, University of Minnesota Medical School, Minneapolis R. Tycko, National Institutes of Health, Bethesda, Maryland



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# **SESSION 1**

- Chairperson: K. Ashe, University of Minnesota Medical School, Minneapolis
- S. Lesné, University of Minnesota, Minneapolis: Breaking the biological code of amyloid-β oligomers.
- D. Eisenberg, University of California, Los Angeles: Structure of the toxic core of  $\alpha$ -synuclein amyloid, the protein associated with the development of Parkinson's disease.
- D. Walsh, Harvard University, Boston, Massachusetts: Amyloid- $\beta$  and beyond: Studies using human brain, cell lines, and recombinant peptides.

### **SESSION 2**

- Chairperson: J. Kelly, Scripps Research Institute, La Jolla, California
- R. Tycko, National Institutes of Health, Bethesda, Maryland: Molecular structures and structural variations in amyloid-β fibrils.
- Y. Ishii, University of Illinois, Chicago: In vitro and in vivo structures of  $A\beta$ (1-42) fibrils and spherical oligomers.
- T. Härd, Swedish University of Agricultural Sciences, Uppsala, Sweden: Solid-state NMR and molecular modeling provide structural information on amyloid-β protofibrils.
- R. Sperling, Harvard University, Boston, Massachusetts: Evolution of preclinical Alzheimer's disease: Implications for secondary prevention trials in Alzheimer's disease.

**General Discussion** 

### **SESSION 3**

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Chairperson: R. Tycko, National Institutes of Health, Bethesda, Maryland

J. Kelly, Scripps Research Institute, La Jolla, California: Toward a structure-proteotoxicity relationship in the transrhyretin amyloidoses.

- J. Collinge, University College London, United Kingdom: Interaction between prion protein and amyloid-β assemblies: Biological significance and therapeutic targeting.
- W. Qiang, Binghamton University, New York: Membrane disruption induced by the β-amyloid peptides.
- R. Nussinov, National Institutes of Health, Leidos Biomedical Research, Frederick, Maryland: Disordered amyloidogenic peptides may insert into the membrane and assemble into common cyclic structural motifs.

### **General Discussion**

### **SESSION 4**

Chairperson: D. Eisenberg, University of California, Los Angeles

K. Ashe, University of Minnesota Medical School, Minneapolis: Temporal, spatial, and structural relationships of type-1 and type-2 amyloid-β oligomers.

- T. Knowles, University of Cambridge, United Kingdom: Kinetics of protein aggregation.
- D. Knopman, Mayo Clinic, Rochester, Minnesota: The detection of suspected non-Alzheimer pathophysiology in cognitively normal persons and implications for the pathogenesis of Alzheimer's disease.

General Discussion

### **SESSION 5**

Chairperson: R. Nussinov, National Institutes of Health, Leidos Biomedical Research, Frederick, Maryland

- J. Nowick, University of California, Irvine: X-ray crystallographic structures of oligomers of peptides derived from amyloid-β.
- C. Soto, University of Texas Medical School, Houston: Detection of amyloid- $\beta$  oligomers in human CSF and blood through amplification of seeding.



J. Collinge

T. Knowles



- B. Ma, National Institutes of Health, Leidos Biomedical Research, Frederick, Maryland: The known and unknown structural aspects of amyloid- $\beta$  peptide globular oligomers.
- R. DeMattos, Eli Lilly and Company, Indianapolis, Indiana: In vivo insights into soluble Aβ dynamics: Lessons from immunotherapy studies targeting soluble versus insoluble Aβ.

**Review and Summary** 



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P. Liu, K. Ashe

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# Creating Patient-Specific Neural Cells for the In Vitro Study of Brain Disorders

# April 14-17

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FUNDED BY Cold Spring Harbor Laboratory Corporate Sponsor Program

ARRANGED BYF. Gage, Salk Institute for Biological Studies, San Diego, CaliforniaR. Jaenisch, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts

Most of the studies of human brain and neuronal function in phenotypically normal and neurological/psychiatric patients have been performed using noninvasive imaging methods that do not give single-cell resolution or performed on postmortem tissues often representing the end-stage of life and disease. The recent advances in reprogramming somatic cells, including the production of induced pluripotent stem cells and induced neuronal phenotypes, have changed the experimental landscape and opened new possibilities. However, a number of pressing issues need to be resolved if this strategy is to become standard for clinically relevant modeling of neurological/psychiatric diseases. For example, more and better protocols are needed for differentiating patient-specific neural cells into specific subtypes. Participants in this Banbury meeting examined some of these issues, including the advantages and disadvantages of the various techniques being used to generate neural cells and how to obtain disease-relevant subtypes of neurons.



R. Jaenisch

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

Opening Remarks and Overviews: F. Gage, Salk Institute for Biological Studies, San Diego, California R. Jaenisch, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts



### **SESSION 1:** Epigenetics

- J. Wu, Salk Institute for Biological Studies, La Jolla, California: A molecular and cellular toolbox for studying brain disorders.
- N. Benvenisty, Hebrew University of Jerusalem, Givat Ram, Jerusalem: Modeling epigenetic disorders using human pluripotent stem cells.
- R. McKay, Lieber Institute for Brain Development, Baltimore, Maryland: Using the dynamic variation between pluripotent stem cells to define the biology of individual human genomes.

### SESSION 2: New Strategies

- D. Panchision, National Institute of Mental Health, Bethesda, Maryland: Next steps in NIMH support for reprogrammed cell research.
- O. Bruestle, University of Bonn, Germany: Toward industrialization of stem-cell-based disease modeling and drug development.
- A. Ebert, Medical College of Wisconsin, Milwaukee: Methods for generating more purified astrocyte cultures from iPSCs.
- P. Vanderhaeghen, University of Brussels, Belgium: From pluripotent stem cells to cortical circuits.
- M. Lancaster, Austrian Academy of Science, Vienna, Austria: Using cerebral organoids to examine pathogenesis of neurodevelopmental disorders.
- F. Vaccarino, Yale University, New Haven, Connecticut: Telencephalic organoids model early developmental trajectories in autism.

### SESSION 3: Modeling Developmental/Psychiatric Diseases

- K. Brennand, Mount Sinai School of Medicine, New York: Modeling predisposition to schizophrenia using hiPSCs.
- C. Marchetto, Salk Institute for Biological Studies, La Jolla, California: Modeling human complex neurological disorders using neural cells.

- E. Morrow, Brown University, Providence, Rhode Island: Live cell imaging of neurodevelopment in cells from patients with Christianson syndrome.
- A. Sawa, Johns Hopkins University School of Medicine, Baltimore, Maryland: Multifaceted clinical study in psychiatry that utilizes patient stem cells.
- H. Song, Johns Hopkins University School of Medicine, Baltimore, Maryland: Patient-derived iPSC modeling of major psychiatric disorders.
- A. Muotri, University of California, San Diego: Clearance of endogenous L1 retroelements in the cytosol by TREX1 prevents neuronal toxicity.

# SESSION 4: Modeling Neurological Diseases

- R. Jaenisch, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts, and F. Soldner, Whitehead Institute, MIT, Cambridge, Massachusetts: In vitro modeling of complex neurological disease.
- R. Livesey, Gurdon Institute, Cambridge, United Kingdom: Insights into mechanisms of Alzheimer's disease pathogenesis from human stem cell models.
- M. McConnell, University of Virginia School of Medicine, Charlottesville: hiPSC-based neurogenesis to study brain mosaicism.
- A. Kaykas, Novartis Institute for BioMedical Research, Cambridge, Massachusetts: A pipeline to identify phenotypes in hPSC-derived neurons.
- L. Rubin, Harvard University, Cambridge, Massachusetts: Spinal muscular atrophy: New insights into a monogenic disorder using patient-derived motor neurons.
- L. Studer, Memorial Sloan Kettering Cancer Center, New York: Modeling neural development and disease in human pluripotent stem cells.
- S. Temple, Neural Stem Cell Institute, Rensselaer, New York: Using iPSCs to model age-related macular degeneration.

**Review and Summary** 



R. McKay, D. Stewart, J. Witkowski, H. Heimer



# Neuronal Response Variability and Correlation

# April 19-22

ARRANGED BY

FUNDED BY The Swartz Foundation

L. Abbott, Columbia University, New York K. Rajan, Princeton University, New Jersey J. Reynolds, Salk Institute for Biological Studies, La Jolla, California

This meeting brought together experimentalists and theorists seeking to understand neuronal response variability and its implications for cortical computation: Is variability "noise" or is it a signature of important computations that we have yet to understand? Participants examined related questions such as how these response fluctuations emerge and how are they modulated by cognitive state, such as attentional state. Variability and correlations are extremely important probes into the workings of neural circuits, but what is the precise relationship between the state and dynamics of a neural circuit and the variability and correlations observed in experiments?



K. Rajan, C. Bargmann

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



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# **SESSION 1**

- D. Angelaki, Baylor College of Medicine, Houston, Texas: How can single sensory neurons predict perception?
- S. Fusi, Columbia University School of Medicine, New York: High dimensional neural representations.
- B. Doiron, University of Pittsburgh, Pennsylvania: Network mechanisms for the control of noise correlations in recurrent cortical populations.
- M. Murthy, Princeton Neuroscience Institute, New Jersey: Rapid sensorimotor integration and song variability in *Drosophila*.

### **SESSION 2**

- M. Fee, Massachusetts Institute of Technology, Cambridge: Dedicated circuits for the generation and shaping of neuronal variability underlying vocal learning in the songbird.
- A. Fairhall, University of Washington, Seattle: Context-dependent modulation of variability through a basal ganglia circuit.
- M. Crair, Yale University School of Medicine, New Haven, Connecticut: Do activity correlations drive circuit development?
- W. Bialek, Lewis-Sigler Institute for Integrative Genomics, Princeton, New Jersey: From correlations to collective activity: Lessons from the retina and explorations beyond.

### **SESSION 3**

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K. Harris, University College London, United Kingdom: Coupling of single neurons to populations in sensory cortex.

- A. Nandy, Salk Institute for Biological Studies, La Jolla, California: Optogenetically induced low-frequency correlations impair perception.
- A. Kohn, Albert Einstein College of Medicine, Bronx, New York: A role for coordinated neuronal activity in corticocortical signaling.
- B. Cumming, National Eye Institute, National Institutes of Health, Bethesda, Maryland: Correlated noise that reflects psychophysical task instructions.

### **SESSION 4**

- C. Bargmann, The Rockefeller University, New York: Variation and circuit states in probabilistic behaviors.
- R. Goris, New York University, Center for Neural Science, New York: Modeling neuronal variability in macaque visual cortex.
- J. Freeman, HHMI, Janelia Farm Research Campus, Ashburn, Virginia: Measuring and manipulating neural computation.
- J. Cunningham, Columbia University, New York: Finding significant structure in large-scale neural recordings.

### **SESSION 5**

- T. Engel, Stanford University, California: Modulation of cortical state by selective visual attention.
- A. Thiele, Newcastle University, Newcastle upon Tyne, United Kingdom: Efficient decoding in the face of response variability.
- B. Hansen, Salk Institute, La Jolla, California: Neural mechanisms underlying attention-related changes in brain state.
- A. Mitra, Washington University School of Medicine, St. Louis, Missouri: The restless brain: How intrinsic activity organizes brain function.



K. Harris



# Beyond the Wheat Genome

April 2	25-27
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FUNDED BY	The Genome Analysis Centre, Norwich, United Kingdom
ARRANGED BY	M. Caccamo, The Genome Analysis Centre, Norwich, United Kingdom

In 2014, the wheat genome project reached a significant milestone with the publication of the first whole-genome reference assembly, although this reference still requires much work. This group convened to examine both the tasks that remain and whether forming an Expert Working Group would promote the completion of those tasks. It was decided that such a group would be useful and plans were laid to develop an Expert Working Group.

Opening Remarks and Introduction: M. Caccamo, The Genome Analysis Centre, Norwich, United Kingdom

# **SESSION 1**

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- N. Stein, Leibniz Institute of Plant Genetics and Crop Plants, Gaterslaben, Germany: Barley genome.
- D. Edwards, University of Western Australia, Crawley, and C. Pozniak, University of Saskatchewan, Saskatoon, Canada: Wheat chromosome assembly.
- E. Akhunov, Kansas State University, Manhattan: Wheat natural diversity.

K. Krasileva, The Genome Analysis Centre, Norwich, United Kingdom and C. Uauy, John Inness Centre, Norwich, United Kingdom: Wheat tilling resources.

A. Hall, University of Liverpool, Liverpool, United Kingdom and M. Bevan, John Innes Centre, Norwich, United Kingdom: Wheat epigenetics.

- K. Mayer, Helmholtz Zentrum München, Neuherberg, Germany: Annotation resources.
- P. Kersey, European Bioinformatics Institute, Cambridge, United Kingdom, and D. Ware, Cold Spring Harbor Laboratory: Bioinformatics resources.

SESSION 2: Breakout Groups: Topics for Discussion

- A. Innovative strategies for improving the genome sequence.
- B. Resequencing wheat genomes.
- C. Functional genomics resources.
- D. Creating a gene expression atlas.
- E. Epigenetic analyses.
- F. Databases and open access data standards.



### Beyond the Wheat Genome 21



M. Bevan, R. McCombie

### SESSION 3: Reports from Breakout Groups

### Group 1

- M. Caccamo, The Genome Analysis Centre, Norwich, United Kingdom
- K. Mayer, Helmholtz Zentrum München, Neuherberg, Germany
- A. Hall, University of Liverpool, United Kingdom
- C. Pozniak, University of Saskatchewan, Saskatoon, Canada

### Group 2

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- E. Akhunov, Kansas State University, Manhattan
- K. Krasileva, The Genome Analysis Centre, Norwich, United Kingdom
- M. Bevan, John Innes Centre, Norwich, United Kingdom

- J. Batley, University of Western Australia, Crawley
- N. Hall, University of Liverpool, United Kingdom
- P. Kersey, European Bioinformatics Institute, Cambridge, United Kingdom

### Group 3

- R. McCombie, Cold Spring Harbor Laboratory
- M. Clark, The Genome Analysis Centre, Norwich, United Kingdom
- C. Uauy, John Innes Centre, Norwich, United Kingdom
- D. Edwards, University of Western Australia, Crawley
- S. Sukumaran, CIMMYT, El Batán, Mexico
- D. Ware, Cold Spring Harbor Laboratory

Discussion and Next Steps



C. Pozniak, D. Edwards

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# NIMH Brain Camp VII

# May 1-3

FUNDED BY

National Institute of Mental Health, National Institutes of Health

ARRANGED BY

T. Insel, National Institute of Mental Health, Bethesda, Maryland J. Chung, National Institute of Mental Health, Bethesda, Maryland

Cold Spring Harbor Laboratory is renowned worldwide for its education programs, from high school level to the highest professional levels. One of the Banbury Center's contributions is to host the NIMH-sponsored "Brain Camp." The goal of the Brain Camp is to identify areas of neuroscience that are of interest and relevance to psychiatrists and to communicate these to a small group of outstanding psychiatry residents and research fellows. Some of the most distinguished and thoughtful neuroscientists in the country came as guest speakers to the meeting. The goal of the series of meetings is to develop a neuroscience curriculum that can eventually be shared with psychiatry training programs around the country.





### **SESSION 1**

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T. Insel, National Institute of Mental Health, Bethesda, Maryland: Will psychiatry become clinical neuroscience? C. Liston, Weill Cornell Medical College, New York: Mecha-

nisms of prefrontal cortical circuit dysfunction in chronic stress and depression.

# **SESSION 2**

S. Amara, National Institute of Mental Health, Bethesda, Maryland: Neurotransmitter transporters: A few curious



observations, many interesting collaborations...and a little advice.

- F. Lee, Weill Cornell Medical College, New York: A vertically integrated approach to studying genetic alterations in psy-chiatric disorders.
- J. LeDoux, New York University, New York: Coming to terms with fear and anxiety.
- T. Jovanovic, Emory University School of Medicine, Atlanta, Georgia: The brain on trauma: Neurobiological correlates of trauma exposure in an urban population.

Roundtable Discussion on Teaching Neuroscience to Psychiatrists

D. Ross, Yale University, New Haven, Connecticut

E. Rosemond, National Institute of Mental Health, Bethesda, Maryland: NIMH funding for M.D. and M.D.-Ph.D.s.

# **SESSION 3**

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- S. Hollingsworth Lisanby, Duke University School of Medicine, Durham, North Carolina: Space, time, and context: The "when," "where," and "how" of focal neuromodulation in psychiatry.
- C. Zarate, National Institute of Mental Health, Bethesda, Maryland: Developing rapid acting antidepressants: Major hurdles, current progress, and future strategies.



F. Lee, L. Bevilacqua

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# Thriving with Schizophrenia

June 14-17

FUNDED BY The Margaret Clark Morgan Foundation

ARRANGED BY L. Dixon, Columbia University, New York H. Heimer, Schizophrenia Research Forum, Providence, Rhode Island J. Kane, North Shore LIJ Health System, Glen Oaks, New York M. Munetz, Northeast Ohio Medical University, Rootstown, Ohio R. Heinssen, National Institute of Mental Health, Bethesda, Maryland

The lives of many people with schizophrenia could be radically improved if they had full access to proven treatments and support services. There have been strong calls for full implementation of the Mental Health Parity Act passed by the U.S. Congress in 2008, especially in the context of the Affordable Care Act of 2010. However, it has been difficult to identify which treatments are effective and which can be widely deployed. The participants in this meeting reviewed and critically evaluated current therapies and support programs for schizophrenia that can or may improve quality of life. Among the topics discussed were pharmacologic therapy, rehabilitation through cognitive training and environmental support, holistic healthcare, and social aspects of therapy.

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

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

**SESSION 1:** Assessing Knowledge about Treatment and Support for People with Schizophrenia

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



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### Thriving with Schizophrenia 25

- L. Dixon, Columbia University, New York: The PORT process: Overview and psychosocial treatments.
- R. Buchanan, Maryland Psychiatric Research Center, Baltimore: PORT: Pharmacologic treatment.
- T. Wykes, Institute of Psychiatry, London, United Kingdom: NICE guidelines.

#### **Discussants Present Key Points**

D. Addington, University of Calgary, Canada

- J. Kane, North Shore-LIJ Health System, Glen Oaks, New York
- L. Davidson, Yale University, New Haven, Connecticut

SESSION 2: Focus on Topical Issues: What Is the Evidence?

Chairperson: M. Munetz, Northeast Ohio Medical University, Rootstown, Ohio

Issue 1: Medication: Balancing Good and Harm

- J. Kane, Hofstra North Shore-LIJ School of Medicine, Glen Oaks, New York
- Issue 2: Cognitive Behavioral Therapy: For What and for Whom?

T. Wykes, Institute of Psychiatry, London, United Kingdom P. McKenna, University of Barcelona, Spain

Issue 3: Supportive Services: Peer Networks, Housing, Employment

M. Chinman, Rand Corporation, Pittsburgh, Pennsylvania L. Davidson, Yale University, New Haven, Connecticut Issue 4: First-Episode Research: Lessons for Schizophrenia

J. Kane, North Shore-LIJ Health System, Glen Oaks, New York D. Addington, University of Calgary, Canada

### SESSION 3: Real-World Laboratories

Chairperson: J. Kane, North Shore-LIJ Health System, Glen Oaks, New York

- M. Munetz, Northeast Ohio Medical University, Rootstown: BeST Program.
- L. Dixon, Columba University, New York: Center for Practice Innovations.
- E. Granholm, University of California, San Diego: Recovery Research Center.
- **SESSION 4:** Barriers to Dissemination and Implementation: What Do We Want to Achieve?
- Chairperson: R. Heinssen, National Institute of Mental Health, Bethesda, Maryland

### Short Presentations

- L. Sederer, Columbia University, New York
- L. Rosenberg, National Council for Behavioral Health, Washington, DC
- A. Sperling, National Alliance on Mental Illness, Arlington, Virginia

### Discussants

- K. Myrick, Substance Abuse and Mental Health Services Administration, Rockville, Maryland
- L. Herman, Northeast Ohio Medical University, Rootstown, Ohio
- F. Frese, Northeast Ohio Medical University, Hudson, Ohio

### General Discussion

### SESSION 5: Getting to Where We Need to Be

Chairpersons: J. Kane, North Shore-LIJ Health System, Glen Oaks, New York, and R. Heinssen, National Institute of Mental Health, Bethesda, Maryland



F. Frese

T. Wykes, L. Sederer

# Integrated Translational Science Center Workshop

# June 18-20

FUNDED BY

ARRANGED BY

L. Baker, University of Michigan, Ann Arbor

National Cancer Institute and The Hope Foundation

L. Ellis, University of Texas, Houston

E. Liu, The Jackson Laboratory, Bar Harbor, Maine

A. Schott, University of Michigan, Ann Arbor

D. Tuveson, Cold Spring Harbor Laboratory

The Integrated Translational Science Center (ITSC) Workshop included clinician scientists from SWOG and basic scientists from Cold Spring Harbor Laboratory (CSHL) and the Jackson Laboratory (JAX). Its goal was to foster interactions between science in the clinic and at the bench. This was an interactive workshop with talks, posters, laboratory demonstrations, and brainstorming sessions to generate ideas for collaborative projects.

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

SESSION 1: Core Strengths

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- D. Tuveson, Cold Spring Harbor Laboratory: Cold Spring Harbor Laboratory: Core strengths.
- E. Liu, The Jackson Laboratory, Bar Harbor, Maine: Jackson Laboratory: Core strengths.
- L. Baker, University of Michigan, Ann Arbor: Workshop Overview.



A. Schott



# Integrated Translational Science Center Workshop 27

# POSTER SESSION

SESSION 2: Lectures by Scientists

- D. Tuveson, Cold Spring Harbor Laboratory: Tissue models/ organoids.
- J. Hicks, Cold Spring Harbor Laboratory: Single-cell analysis.
- E. Liu, The Jackson Laboratory, Bar Harbor, Maine: JAX animal models, PDX mouse, and genomics technologies.

# POSTER SESSION

SESSION 3: Demonstrations of the Techniques Discussed

# Organoids

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- L. Baker, Cold Spring Harbor Laboratory
- D. Engle, Cold Spring Harbor Laboratory

# D. Ohlund, Cold Spring Harbor Laboratory

# Single-Cell Analysis

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- J. Hicks, Cold Spring Harbor Laboratory
- J. Alexander, Cold Spring Harbor Laboratory
- J. Kendall, Cold Spring Harbor Laboratory

# JAX Platforms (All): Humanized Mice, PDX, Genomics Platforms

J. Keck, The Jackson Laboratory

A. Cheng, The Jackson Laboratory

P. Robson, The Jackson Laboratory

SESSION 4: CSHL Campus Tour

SESSION 5: ITSC Pilot Submission Process: How to Write a Successful Proposal



C. Bult, P. Robson

# Mitochondria and Cancer

# September 1-4

funded by	Oliver Grace Cancer Fund
ARRANGED BY	N. Chandel, Northwestern University

N. Chandel, Northwestern University, Chicago, Illinois D. Sabatini, Whitehead Institute, Massachusetts Institute of Technology, Cambridge

Cancer cells rely on mitochondrial metabolism to provide the necessary building blocks for macromolecule (nucleotides, lipids, amino acids) synthesis as well as ATP and NADPH essential for cell proliferation. Multiple substrates feed mitochondrial metabolism, including pyruvate and glutamine. As a consequence of oxidative metabolism, the mitochondria of cancer cells produce significant amounts of ROS to activate proximal signaling pathways and promote tumorigenesis. Although the majority of cancer cells display functional mitochondria, there are small subsets of cancer cells with impaired mitochondrial function. Despite the inability to generate mitochondrial ATP, these cancer cells demonstrate remarkable metabolic plasticity, allowing them to conduct biosynthetic functions for macromolecule synthesis. Overall, the accumulating evidence now suggests that mitochondrial bioenergetics, biosynthesis, and signaling are required for tumorigenesis. Thus, emerging studies have begun to unveil the targeting of mitochondrial metabolism as a promising avenue for cancer therapy.

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

Introduction and Goals of Workshop: N. Chandel, Northwestern University, Chicago, Illinois



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### SESSION 1: Mitochondrial Metabolism of Cancer Cells In Vivo

- Chairperson: E. Gottlieb, Cancer Research UK Beatson Institute, Glasgow, United Kingdom
- T. Fan, University of Kentucky, Lexington: Human lung cancer metabolome, from bench to bedside.
- M. VanderHeiden, Massachusetts Institute of Technology, Cambridge: Role of respiration in cancer cell proliferation.
- S. Demo, Calithera Biosciences, Inc., South San Francisco, California: Identification of biomarkers of sensitivity to the glutaminase inhibitor, CB-839.

### SESSION 2: Mitochondria and Metabolic Stress

- **Chairperson: J. Rutter**, University of Utah School of Medicine, Salt Lake City
- E. White, Rutgers University, New Brunswick, New Jersey: Mitochondrial quality control and cancer.
- K. Macleod, University of Chicago, Illinois: Deregulation of mitophagy and altered mitochondrial mass in cancer.
- W. Gu, Columbia University, New York: p53-mediated ferroptosis in ROS responses, tumor suppression, and premature aging.

### SESSION 3: Mitochondrial Metabolites and Cancer

- Chairperson: E. White, Rutgers University, New Brunswick, New Jersey
- Marcia Haigis, Harvard Medical School, Boston, Massachusetts: PHD3 and fat metabolism.
- E. Gottlieb, Cancer Research UK Beatson Institute, Glasgow, United Kingdom: Metabolic adaptations and liabilities of TCA cycle-truncated tumors.
- K. Wellen, University of Pennsylvania, Philadelphia: Mitochondrial metabolism and regulation of nuclear gene expression in cancer.

SESSION 4: Mitochondria and Aging

- Chairperson: E. White, Rutgers University, New Brunswick, New Jersey
- J. Auwerx, Ecole Polytechnique Federale de Lausanne, Switzerland: Mitonuclear communication in metabolism and aging.
- A. Brunet, Stanford University, California: Metabolic and epigenetic regulation of aging.
- General Discussion: M. Espey, National Cancer Institute, Rockville, Maryland

SESSION 5: Biology of Complex I

- Chairperson: K. Salnikow, National Cancer Institute, NIH, Rockville Maryland
- D. Sabatini, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts: Systematic approaches to study metabolism.
- M. Kaeberlein, University of Washington, Seattle: Identification of interventions that delay mitochondrial disease in Complex-I-deficient mice.
- SESSION 6: Targeting Mitochondrial Electron Transport Chain
- Chairperson: K. Salnikow, National Cancer Institute, NIH, Rockville, Maryland.
- N. Chandel, Northwestern University, Chicago, Illinois: Dissecting biology of respiratory complexes.
- L. Trotman, Cold Spring Harbor Laboratory: Mitochondria and prostate metastasis.
- G. Draetta, MD Anderson Cancer Center, Houston, Texas: OXPHOS inhibitors as cancer therapeutics.



J. Watson, E. White

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D. Sykes, Massachusetts General Hospital, Boston: Targeting DHODH and endogenous uridine biosynthesis in the treatment of patients with acute myeloid leukemia.

### SESSION 7: Regulators of Mitochondrial Metabolism

- Chairperson: E. White, Rutgers University, New Brunswick, New Jersey
- J. Rutter, University of Utah School of Medicine, Salt Lake City: The impact of pyruvate metabolism on stemness in normal and cancer settings.
- C. Metallo, University of California, San Diego, La Jolla: Mitochondria and amino acid metabolism.
- D. Altieri, The Wistar Institute, Philadelphia, Pennsylvania: Regulators of mitochondrial metabolism and cancer therapy.

### SESSION 8: Mitochondria Regulation of Adaptive Immunity

- Chairperson: M. Haigis, Harvard Medical School, Boston, Massachusetts
- P. Ashton-Rickardt, Imperial College London, United Kingdom: The protein LEM promotes CD8+ T-cell immunity through effects on mitochondrial respiration.

J. Powell, Johns Hopkins University, Baltimore, Maryland: Dissecting and exploiting metabolism in T cells.

General Discussion: M. VanderHeiden, Massachusetts Institute of Technology, Cambridge

### SESSION 9: Mitochondria and ATM-p53 Pathway

- Chairperson: N. Chandel, Northwestern University, Chicago, Illinois
- M. Kastan, Duke Cancer Institute, Durham, North Carolina: ATM: Bridging DNA damage responses and metabolic regulation.
- P. Hwang, National Heart, Lung & Blood Institute, Bethesda, Maryland: Targeting mitochondria for cancer prevention in Li-Fraumeni syndrome.
- R. Sordella, Cold Spring Harbor Laboratory: p53' evil twin linked to tissue injury and spread of cancer.
- A. Yang, Boston Biomedical Inc., Cambridge, Massachusetts: BBI-608 targets cancer stem cells and prevents tumor relapse and metastasis.
- Meeting Summary: N. Chandel, Northwestern University, Chicago, Illinois



J. Auwerx

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# Therapeutic Approaches to Prion Disease and Other Neurodegenerative Conditions Associated with Protein Misfolding

September 15-18

FUNDED BYCold Spring Harbor Laboratory Corporate Sponsor ProgramARRANGED BYJ. Collinge, University College London, United Kingdom<br/>J. Kelly, The Scripps Research Institute, La Jolla, California

Neurodegenerative diseases such as Alzheimer's disease arguably represent the greatest challenge to healthcare systems in developed countries with aging populations, and as yet no effective disease-modifying therapies are available. Major advances in understanding prion disease, a rare but high-profile cause of dementia, are now leading to the development of therapeutics. In parallel, it is becoming clear that similar molecular processes of protein misfolding and aggregation ("prionlike mechanisms") are involved in the much commoner dementias such as Alzheimer's disease. Participants in this meeting examined progress in development of therapeutics for prion diseases and other potentially tractable protein misfolding disorders and considered their wider relevance for diseases of major public health and economic importance.

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

Meeting Introduction: J. Collinge, University College London, United Kingdom J. Kelly, The Scripps Research Institute, La Jolla, California

Introduction to Prion-Like Mechanisms and Relevance to Human Neurodegenerative Disease: J. Collinge, University College London, United Kingdom

SESSION 1: Small-Molecule Therapeutics for Prion Disease

Chairperson: J. Collinge, University College London, United Kingdom

B. Caughey, NIAID Rocky Mountain Laboratories, Hamilton, Montana: Practical detection of prions and prion inhibitors.

- M. Farrow, University College London, United Kingdom: Development of a clinical candidate drug for treatment of prion disease.
- G. Legname, Scuola Internazionale Superiore di Studi Avanzati, Trieste, Italy: Tackling prion diseases with multitarget and theranostic small molecules.



- K. Kuwata, Gifu University, Japan: Toward a first in human trial of a medical chaperone for prion disease.
- A. Giese, Ludwig-Maximilians-University, Munich, Germany: Targeting toxic oligomers with small molecules: Chances and challenges.

General Discussion: Key Issues in Developing Small-Molecule Therapeutics

SESSION 2: Immunotherapeutic Approaches

Chairperson: F. Tagliavini, Instituto Neurologico Carlo Besta, Milan, Italy

- C. Glabe, University of California, Irvine: Anti-amyloid antibodies: What do they see that we don't?
- J. Collinge, University College London, United Kingdom: Passive immunotherapy of prion disease.

T. Wisniewski, New York University School of Medicine, New York: Vaccination approaches for prion and Alzheimer's disease.

M. Horiuchi, Hokkaido University, Sapporo, Japan: Immunoand cell therapy as possible treatments for prion disease.

General Discussion: Key Issues in Immunotherapeutic Approaches

### SESSION 3: Alzheimer's and Tauopathies

- Chairperson: D. Walsh, Brigham and Women's Hospital, Boston, Massachusetts
- D. Walsh, Brigham and Women's Hospital, Boston, Massachusetts: The activity and forms of  $A\beta$  in mild AD brains.
- A. Nicoll, UCL Institute of Neurology, London, United Kingdom: Dissecting the PrP:Aβ interaction.

- S. Strittmatter, Yale University School of Medicine, New Haven, Connecticut: Cellular prion protein signal transduction complex mediating amyloid-β oligomer synaptotoxicity in Alzheimer's disease.
- M. Hutton, Eli Lilly and Company Ltd., Surrey, United Kingdom: Tau pathology: Critical Tau species required for propagation and spreading.
- F. Tagliavini, Instituto Neurologico Carlo Besta, Milan, Italy: Novel approach to Alzheimer's disease therapeutics based on a natural variant of A- $\beta$  that hinders amyloidogenesis.
- S. Olson, University of California Institute for Neurodegenerative Diseases, San Francisco: A high-content assay approach to drug discovery for neurodegenerative disorders.

General Discussion: Key Issues in Alzheimer's and Tauopathies

SESSION 4: Proteostasis, Protein Misfolding, and Therapeutic Approaches to Neurodegenerative Diseases

- Chairperson: J. Kelly, The Scripps Research Institute, La Jolla, California
- A. Horwich, Yale University, New Haven, Connecticut: Studies of mice with SOD-1-linked ALS.
- R. Morimoto, Northwestern University, Evanston, Illinois: Epigenetic regulation of proteostasis networks in stress, aging, and disease.
- J. Kelly, The Scripps Research Institute, La Jolla, California: Adapting proteostasis to ameliorate degenerative diseases.
- Closing Remarks: J. Collinge, University College London, United Kingdom, and J. Kelly, The Scripps Research Institute, La Jolla, California



A. Horwich, R. Morimoto

# Therapeutic Use of Ketamine for Treating Severe Depression: Risks and Potential

# September 20-22

FUNDED BY

Cold Spring Harbor Corporate Sponsor Program; Alkermes, Inc.; and Janssen Research & Development

ARRANGED BY R. Robinson Beale, Blue Cross of Idaho, Meridian H. Heimer, Cold Spring Harbor Laboratory J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory

Ketamine is purported to be the only truly new and effective therapy discovered for depression in the past 50 years. Individuals who are severely depressed and often suicidal respond rapidly to the common anesthetic, reporting dramatic mood changes within minutes. The benefits can last for several weeks, giving other standard therapies an opportunity to take effect. Despite this, ketamine is not widely available. This meeting convened representatives from academia, government, and private payers, as well as patient advocates, to discuss the risks and possibilities presented by broader use of ketamine for treating severe depression.

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



H. Heimer, A. Malhotra

Meeting Introduction: H. Heimer, Cold Spring Harbor Laboratory



SESSION 1: Current Knowledge and Ongoing Research

- Chairperson: S. Mathew, Baylor College of Medicine, Houston, Texas
- D. Charney, Icahn School of Medicine, New York, and M. Fava, Massachusetts General Hospital, Boston: Ketamine in depression: Clinical trial evidence.
- G. Sanacora, Yale University, New Haven, Connecticut: Lessons from other proposed rapidly acting antidepressants: Pharmacological specificity and nonspecific clinical effects.
- E. Ehrich, Alkermes, plc, Waltham, Massachusetts: Opioid modulation as a treatment of major depressive disorder.
- C. Nemeroff, University of Miami, Florida: Meta-analysis of ketamine and related compounds in depression.

### Where Next for Research?

- A. Schatzberg, Stanford University, California
- M. Hillefors, National Institute of Mental Health, Bethesda, Maryland
- General Discussion and Summation: Five Key Points Relating to Current Knowledge and Research

#### SESSION 2: Current Clinical Practice and Challenges

- Chairperson: R. Robinson Beale, Blue Cross of Idaho, Meridian, Idaho
- A. Dahan, Leiden University Medical Center, Leiden, The Netherlands: Ketamine pharmacokinetics and pharmacodynamics: Efficacy and toxicity.
- G. Brooks, New York Ketamine Infusions, New York: Current clinical practice and challenges.

- S. Levine, Ketamine Treatment Centers, Princeton, New Jersey: Five years of clinical experience with ketamine treatment for depression in an outpatient/private practice setting.
- M. Frye, Mayo Clinic, Rochester, New York: Ketamine clinics for treatment resistant depression: Infrastructure and clinical development.
- M. Turner, Kaiser Permanente, San Francisco, California: The role of ketamine in long-term treatment of depression: Legal, regulatory, and ethical considerations in the use of ketamine.

# General Discussion and Summation: Five Key Points Relating to Current Practice and Challenges

#### SESSION 3: Stakeholder Concerns

- Chairperson: A. Malhotra, North Shore-LIJ Health System, Glen Oaks, New York
- M. Isaac, European Medicines Agency, London, United Kingdom
- D. Hartman, Ketamine Advocacy Network, Seattle, Washington
- P. Summergrad, Tufts Medical Center, Boston, Massachusetts
- R. Robinson Beale, Blue Cross of Idaho, Meridian, Idaho
- I. Wiechers, Office of Mental Health Operations, Department of Veterans Affairs, West Haven, Connecticut

### SESSION 4: Recommendations and Guidelines

# Chairperson: H. Goldman, University of Maryland, Potomac

A. Revisiting Key Issues.





G. Sancora, C. Nemeroff

# Therapeutic Developments for ALS: Antisense, Gene Therapy, and Stem Cells

### September 27–30

FUNDED BYThe Greater New York Chapter of The ALS AssociationARRANGED BYL. Bruijn, The ALS Association, Washington, D.C.<br/>T. Miller, Washington University, St. Louis, Missouri<br/>C. Svendsen, Cedars-Sinai, Los Angeles, California<br/>D. Sah, Voyager Therapeutics, Cambridge, Massachusetts

This workshop discussed the key common challenges in therapeutic development for ALS shared by antisense oligonucleotide, gene therapy, and stem cell modalities, with the goal of identifying steps that will facilitate solutions to these challenges and ultimately enhance the probability of successful clinical development. In particular, translation of delivery, biomarker development, trial design, and regulatory issues was highlighted. These challenges are especially relevant this year with the important progress anticipated in bringing antisense therapy closer to the clinic for SOD1 and C9orf72, and in advancing stem cell therapies already in clinical trials or planned for later this year. Clinicians, scientists, and regulatory experts provided overviews of the current status of the various antisense oligonucleotide, gene therapy, and stem cell programs, setting the stage for discussions around the key common challenges: translation of delivery, biomarker development, trial design, and regulatory issues.

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

Overview and Workshop Goals: L. Bruijn, ALS Association, Washington, D.C.



SESSION 1: Antisense Oligonucleotide Therapy

Chairperson: T. Miller, Washington University, St. Louis, Missouri

T. Miller, Washington University, St. Louis, Missouri: SOD1.

D. Cleveland, University of California, San Diego: C9orf72.

D. Rodman, miRagen Therapeutics, Boulder, Colorado: microRNA targeting to the CNS.

General Discussion, Highlighting Key Points

### SESSION 2: Gene Therapy

Chairperson: R. Bartus, RTBioconsultants, Inc., San Diego, California

K. Bankiewicz, University of California, San Francisco

B. Kaspar, Ohio State University, Columbus

D. Sah, Voyager Therapeutics, Cambridge, Massachusetts

### General Discussion Highlighting Key Points

## SESSION 3: Stem Cells

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Chairperson: D. Rowitch, University of California, San Francisco

- J. Glass, Emory University School of Medicine, Atlanta, Georgia: Neuralstem.
- C. Svendsen, Cedars-Sinai Medical Center, Los Angeles, California: CIRM/Cedars-Sinai combined stem and gene therapy trial.

N. Maragakis, Johns Hopkins University School of Medicine, Baltimore, Maryland, and J. Campanelli, Q Therapeutics, Inc., Salt Lake City, Utah: Q therapeutics trial.

General Discussion Highlighting Key Points

SESSION 4: Delivery and Biomarker Development

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

G. Stewart, Voyager Therapeutics, Cambridge, Massachusetts: Lost in (therapy) translation: It won't work, if it doesn't get there.

N. Boulis, Emory University, Atlanta, Georgia, and C. Svendsen, Cedars-Sinai Medical Center, Los Angeles, California: Stem cell tracking techniques and delivery.

E. Ahrens, University of California, San Diego, La Jolla: Emerging MRI methods to assess cell engraftment and host response.

### General Discussion Highlighting Key Points

SESSION 5: Regulatory and Clinical Trial Design Panel Discussion

Chairperson: B. Ravina, Voyager Therapeutics, Cambridge, Massachusetts

## Panelists

J. Lebkowski, Asterias Biotherapeutics, Portola Valley, California

J. Berry, Massachusetts General Hospital, Boston

T. Ferguson, Biogen, Cambridge, Massachusetts

General Discussion Highlighting Key Points

### SESSION 6: Animal Models

- Chairperson: J. Rothstein, Johns Hopkins University School of Medicine, Baltimore, Maryland
- R. Baloh, Cedars-Sinai Medical Center, Los Angeles, California: Overview of mouse models.
- J. Coates, University of Missouri, Columbia: Canine degenerative myelopathy: A potential disease model of ALS.
- A. Burghes, Ohio State University, Columbus: SMA pig model.
- Z. Xu, University of Massachusetts Medical School of Medicine, Worcester: Modeling and treatment of sporadic ALS.

General Discussion Highlighting Key Points Closing Remarks



M. Cudkowicz, N. Boulis

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# What Is Needed to Harness Chemogenetics for the Treatment of Human Brain Disorders?

# October 4-7

FUNDED BYCold Spring Harbor Laboratory Corporate Sponsor ProgramARRANGED BYG. Aston-Jones, Rutgers University and Rutgers Biomedical and Health Sciences, Piscataway,<br/>New Jersey<br/>T. Kash, University of North Carolina, Chapel Hill

Disorders of the brain are widespread and impose a tremendous cost on individuals and society. Despite the enormous toll, we are at a near standstill in the development of new treatments for these conditions. Recent technical developments, including optogenetics and chemogenetics, have allowed scientists to identify specific brain circuit elements in both physiological and pathological behavior. Chemogenetics, a method for manipulating cellular function using drug-like compounds and engineered proteins, has shown promise for probing circuit function and has the potential to bridge the gap between genetic analysis of circuit function and treatment. The goal of this meeting was to bring together experts with broad expertise in neurobiology, tool development, primate biology, neurosurgery, and imaging to identify a clear path forward for the use of chemogenetic tools for treatment of human disease.

Introduction: G. Aston-Jones, Rutgers University, Piscataway, New Jersey

**SESSION 1:** Designing New Chemogenetic Tools

Chairperson: G. Aston-Jones, Rutgers University, Piscataway, New Jersey J. English, University of North Carolina, Chapel Hill: DREADD 2.0: Novel methods for DREADD production and implementation.



- T. Kash, University of North Carolina, Chapel Hill: Potential new approaches to DREADD manipulation of neuronal circuit.
- J. Jin, Icahn School of Medicine at Mount Sinai, New York: The next generation of DREADD ligands.
- J. Wess, National Institute of Neurological Disorders, Bethesda, Maryland: DREADDs with distinct coupling properties: in vitro and in vivo studies.

SESSION 2: New Chemogenetic Approaches with Potential Clinical Applications

Chairperson: E. Vazey, University of Massachusetts, Amherst

- Y. Hurd, Icahn School of Medicine at Mount Sinai, New York: DREAMM for in vivo pathway-specific brain activity mapping.
- S. Dymecki, Harvard Medical School, Boston, Massachusetts: Conditional DREADD knock-in alleles: Lessons from mice.
- R. Adan, Utrecht University, The Netherlands: Targeting specific neurons implicated in obesity.
- B. Roth, University of North Carolina, Chapel Hill: Chemical biology of chemogenetic actuators.

**General Discussion** 

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- SESSION 3: Using Chemogenetics to Probe Neuronal Circuit Function and Dysfunction
- Chairperson: K. Grant, Oregon National Primate Research Center, Beaverton
- G. Aston-Jones, Rutgers University, Piscataway, New Jersey: Dopamine DREADDs, drug seeking, and demand.
- S. Ferguson, University of Washington, Seattle: Using DREADDs to map addiction circuits.
- B. Li, Cold Spring Harbor Laboratory: Chemogenetic inhibition of the amygdala circuits during fear processing in mice.

E. Vazey, University of Massachusetts, Amherst: Selective manipulation of locus coeruleus norepinephrine circuitry from arousal to attention.

SESSION 4: Optimizing Chemogenetic Approaches in Primates

- Chairperson: T. Kash, University of North Carolina, Chapel Hill
- K. Grant, Oregon National Primate Research Center, Beaverton: Using DREADDs to address functional neurocircuitry and behavioral outcomes in monkeys.
- N. Kalin, University of Wisconsin, Madison: Developing DREADDs methodology in nonhuman primates to reversibly manipulate the neural circuitry underlying anxiety disorders.
- T. Minamimoto, National Institute of Radiological Sciences, Chiba, Japan: PET imaging of DREADDs in monkeys.
- B. Richmond, National Institute of Mental Health, Bethesda, Maryland: The possibilities and problems in controlling cortical connections using DREADDs.

General Discussion

SESSION 5: Making the Leap to Therapy

Chairperson: N. Kalin, University of Wisconsin, Madison

- D. Kullmann, University College London, United Kingdom: Chemogenetics for epilepsy: How far from clinical translation?
- C. Felder, Neuroscience, Eli Lilly & Co., Indianapolis, Indiana: Recent challenges and advances in GPCR drug discovery: Importance of academic-industrial partnerships.
- D. Goldman, National Institute on Alcohol Abuse & Alcoholism, Rockville, Maryland: Chemogenetics for addictions: Challenges and opportunities.

General Discussion and Summary



Y. Hurd



R. Adan, J. Weiss

# HIV-1 and How to Kill a Killer: Attempts at Total or Functional Cure of HIV-1

# October 13-16

FUNDED BY amfAR; The Foundation for AIDS Research; Gilead Sciences, Inc.; and Office of AIDS Research, NIH, NIDA, and NIAID Division of AIDS
 ARRANGED BY R. Gallo, IHV at University of Maryland School of Medicine, Baltimore S. Deeks, University of California, San Francisco R. Siliciano, Johns Hopkins University, Baltimore, Maryland

AIDS led to an extraordinary research effort during the past 30 years, and although much has been learned about the basic biology of HIV and therapies have been developed to combat AIDS, there remain unanswered questions. Two are key in our efforts to develop treatments: Can we obtain a complete virological cure? And, if not, can we obtain a functional cure (no further therapy needed)? A select group of top experts and opinion leaders in the field of HIV pathogenesis came to Banbury to critically examine what has been done and what might be done to answer these questions. Previous Banbury Center meetings on HIV and AIDS (1983, 1988, 1989, 1992) were important and timely, and the 2015 meeting proved to be equally so.



R. Gallo

**Opening Remarks and Questions for the Field: R. Gallo**, IHV at University of Maryland School of Medicine, Baltimore

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



Measuring the Size of the Latent Reservoir: A Key to Successful Eradication Strategies: R. Siliciano, Johns Hopkins University, Baltimore, Maryland

### SESSION 1: Virology

- Chairperson: D. Kuritzkes, Brigham & Women's Hospital, Cambridge, Massachusetts
- J. Coffin, Tufts University, Boston, Massachusetts: Intracellular RNA expression in treated and untreated HIV-infected individuals.
- J. Mellors, University of Pittsburgh, Pennsylvania: Clonal expansion of HIV-1 reservoirs.
- J. Mullins, University of Washington, Seattle: Propagation and comprehensive analysis of individual lineages of HIVinfected cells persisting during ART.
- J.V. Garcia-Martinez, University of North Carolina, Chapel Hill: Systemic distribution of the latent HIV reservoir.
- E. Verdin, University of California, San Francisco: Molecular mechanisms of HIV latency.

### SESSION 2: Immunology

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- Chairperson: P. Sato, NIH Office of AIDS Research, Bethesda, Maryland
- R.-P. Sekaly, Case Western Reserve University, Cleveland, Ohio: Restoring immune homeostasis to eradicate HIV.
- B. Walker, The Ragon Institute, Cambridge, Massachusetts: T-cell-mediated clearance of infected cells.
- W. Greene, Gladstone Institute of Virology and Immunology, San Francisco, California: Death by friendly fire: How HIV turns our innate immune defenses against us.
- J. Ananworanich, US Military HIV Research Program, Bethesda, Maryland: Reservoirs and immune activation in blood and tissue compartments from the RV254 Thai cohort.

### General Discussion Reviewing Key Issues

### SESSION 3: Biomarkers

- Chairperson: D. Finzi, National Institutes of Health, Bethesda, Maryland
- D. Richman, University of California, San Diego: Improving assays to measure the latent reservoir.
- D. Kuritzkes, Brigham & Women's Hospital, Cambridge, Massachusetts: The challenge of identifying surrogate markers for HIV cure.

### SESSION 4: Novel Therapies

- Chairperson: W. Greene, Gladstone Institute of Virology and Immunology, San Francisco, California
- J. Lifson, National Cancer Institute, Frederick, Maryland: The role of NHP models in HIV cure research.
- M. Lichterfeld, Ragon Institute, Cambridge, Massachusetts: Immune mechanisms of HIV-1 reservoir decline during latency-reversing treatment: Lessons from clinical trials.
- A. Garzino-Demo, University of Maryland, Baltimore: Letting sleeping dogs lie: Targeting T-cell activation.
- M. Stevenson, University of Miami, Florida: Strategies other than "purge and kill" to limit viral reservoirs.

#### General Discussion Reviewing Key Issues

### SESSION 5: Latency Reversal

Chairperson: D. Margolis, University of North Carolina, Chapel Hill

D. Hazuda, Merck Research Labs, West Point, Pennsylvania: Understanding the activity of HDACIs in vitro and in vivo.



C. Dieffenbach, E. Verdin

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- J. Karn, Case Western Reserve University, Cleveland, Ohio: Distinct mechanisms of hormonal control of HIV latency in T cells and microglial cells.
- B. Peterlin, University of California, San Francisco: Mechanistic approaches to HIV cure: PKC agonists and latency reversing agents.
- F. Romerio, University of Maryland, Baltimore: The HIV-1 antisense transcript AST is an inducer of viral latency.

General Discussion Reviewing Key Issues

SESSION 6: Experimental Medicine and Clinical Trials

- Chairperson: S. Read, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland
- R. Geleziunas, Gilead Sciences, Inc., Foster City, California: TLR7 agonists for HIV.

- D. Margolis, University of North Carolina, Chapel Hill: Understanding latency reversal and reservoir clearance.
- S. Deeks, University of California, San Francisco: Closing comments: Challenges in translation.

# SESSION 7: Commentary

- R. Gallo, IHV at University of Maryland, Baltimore
- S. Deeks, University of California, San Francisco
- R. Siliciano, Johns Hopkins University, Baltimore, Maryland
- C. Dieffenbach, National Institute of Allergy and Infectious Diseases, Rockville, Maryland
- R. Johnston, amfAR, New York

### General Discussion and Summary

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# The Lustgarten Foundation Scientific Meeting

# October 18-20

FUNDED BY The Lustgarten Foundation

ARRANGED BY C. Ardito-Abraham, The Lustgarten Foundation, Bethpage, New York D. Tuveson, Cold Spring Harbor Laboratory

The Banbury Center is always pleased to provide a venue for the Lustgarten Foundation to hold its annual Pancreatic Cancer Scientific Conference. The occasion provides an opportunity for researchers funded by the Foundation to get together and exchange information and ideas, thus enabling the Foundation scientific advisory board to assess progress in the field and plan for the future.

### Welcome and Introductions

### **Research Investigators Progress Reports**

- S. Leach, Memorial Sloan Kettering Cancer Center, New York S. Lowe, Memorial Sloan Kettering Cancer Center, New York
- C. Fuchs, Dana Farber Cancer Institute, Boston, Massachusetts
- M. Muzumdar, Dana Farber Cancer Institute, Boston,
- Massachusetts F. McCormick, University of California, San Francisco
- T. Jacks, Massachusetts Institute of Technology, Cambridge
- S. Fesik, Vanderbilt University School of Medicine, Nashville,
- Tennessee C. Der, University of North Carolina, Chapel Hill
- G. Verdine, Harvard University, Cambridge, Massachusetts
- L. Cantley, Weill Cornell Medical College, New York
- T. Hunter, Salk Institute for Biological Studies, La Jolla, California
- J. Sage, Stanford University Medical Center, California
- D. Simeone, University of Michigan, Ann Arbor
- A. Klein, Johns Hopkins University School of Medicine, Baltimore, Maryland
- H. Ploegh, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts

# SAB/KRas Discussion

C. Fuchs, Dana Farber Cancer Institute, Boston, Massachusetts F. McCormick, University of California, San Francisco

### **Research Biopsy Study**

B. Wolpin, Dana Farber Cancer Institute, Boston, Massachusetts

### **Distinguished Scholar Progress Reports**

- D. Tuveson, Cold Spring Harbor Laboratory
- R. Evans, Salk Institute for Biological Studies, La Jolla, California
- D. Fearon, Cold Spring Harbor Laboratory
- B. Vogelstein, Johns Hopkins University, Baltimore, Maryland







B. Vogelstein, L. Cantley



C. Ardito-Abraham

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# Scientific and Clinical Foundation for Precision Medicine in Epilepsy

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# November 1-4

funded by	CURE Epilepsy; University of California, San Francisco; Ron and Sanne Higgins Epilepsy Fund; Columbia University Institute for Genomic Medicine; Pairnomix; and Clarus Ventures
ARRANGED BY	<ul> <li>S. Berkovic, Austin Health, University of Melbourne, Heidelberg, Australia</li> <li>E. Heinzen Cox, Columbia University, New York</li> <li>D. Goldstein, Columbia University, New York</li> <li>D. Lowenstein, University of California, San Francisco</li> </ul>

Epilepsy is a common and often devastating neurological disease affecting at least one in 26 Americans at some point in their lives. Critically, more than 30% continue to have seizures despite the many available therapies. Unfortunately, drug development in epilepsy has largely stalled, but epilepsy genetics affords an opportunity to develop new targeted treatments in epilepsy. Participants in this meeting examined progress in the genetics of the epilepsies; the advent of animal and in vitro models allowing the development of medications tailored to genetically defined subtypes of epilepsy; and how to evaluate the efficacy of experimental treatments in cost-effective clinical trials.

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

SESSION 1: Epilepsy Genetics I: Gene Discovery Update

Chairperson: D. Goldstein, Columbia University, New York

S. Berkovic, Austin Health, University of Melbourne, Heidelberg, Australia: Success in genetics and challenges ahead.E. Heinzen Cox, Columbia University, New York: Gene discovery in severe sporadic epilepsies.



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- H. Mefford, University of Washington, Seattle: What we have learned from study of copy-number variants in epilepsy.
- S. Petrovski, Columbia University, New York: Pinpointing epilepsy risk mutations using intolerance scoring.
- K. Samocha, Massachusetts General Hospital, Boston: Genetic analysis approaches in complex neurological disease.
- O. Devinsky, New York University School of Medicine, New York: Diagnostic sequencing in the adult and pediatric settings.
- SESSION 2: Functioning Modeling: Etiology, Excitability Networks and Mechanisms

Chairperson: S. Petrou, Florey Institute of Neuroscience and Mental Health, Melbourne, Australia

- E. Cooper, Baylor College of Medicine, Houston, Texas: Genetics and structure-function implications of Kv7 channels in epilepsy.
- J. Kearney, Northwestern University, Chicago, Illinois: Comparing human vs. mouse sodium channelopathies.
- A. Bassuk, University of Iowa, Iowa City: Precision genetics in multiple species.
- C. Gross, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio: microRNA-mediated regulation of potassium channel complexes in epilepsy.
- M. Weston, Baylor College of Medicine, Houston, Texas: Interneuronal communication in mTOR 'opathies'.
- E. Rossignol, CHU Ste-Justine Research Center, Montreal, Canada: Developmental interneuronopathy and epilepsy.

### SESSION 3: Platforms in Functional Modeling

Chairperson: J. Parent, University of Michigan, Ann Arbor K. Staley, Massachusetts General Hospital, Boston: Organotypic cultures for drug screens.

- W. Frankel, Jackson Laboratory, Bar Harbor, Maine: Recent progress in modeling epilepsy in laboratory mice.
- K. Eggan, Harvard University, Cambridge, Massachusetts: Modeling of neuropsychiatric disease mutations in human neurons.
- A. Cohen, Harvard University, Cambridge, Massachusetts: All-optical electrophysiology for neuronal disease modeling and drug discovery.
- J. Parent, University of Michigan, Ann Arbor: iPSCs in the study of epileptic encephalopathies.
- D. Goldstein, Columbia University, New York: Multielectrode arrays for modeling epilepsy mutations.

General Discussion Reviewing Key Issues

- **SESSION 4:** Developing Effective Epilepsy Therapies from Precision Genetics
- Chairperson: S. Berkovic, Austin Health, University of Melbourne, Heidelberg, Australia
- S. Baraban, University of California, San Francisco: SCN1A: Drug screening in Dravet syndrome zebrafish.
- S. Petrou, Florey Institute of Neuroscience and Mental Health, Melbourne, Australia: SCN1A: Modulation of SCN1A by spider toxin.
- D. Krafte, Icagen, Cambridge, Massachusetts: KCNT1: Investigation of KCNT1 variants associated in childhood epilepsy.
- D. Dlugos, Children's Hospital of Pennsylvania, Philadelphia: KCNT1: Quinidine in KCNT1 epilepsies.
- S. Mullen, Florey Institute of Neuroscience and Mental Health, Melbourne, Australia: KCNT1: A clinical trial for nocturnal frontal lobe epilepsy due to KCNT1 mutation.
- I. Scheffer, Florey Institute and University of Melbourne, Australia: Targeted treatments of PCDH19 related epilepsies and mTORopathies.



H. Mefford, A. Poduri

A. Bassuk, V. Whittemore

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S. Traynelis, Emory University School of Medicine, Atlanta, Georgia: GRIN2A: GRIN2A mutation and early-onset epileptic encephalopathy: Personalized therapy with memantine.

Group Discussion: Reviewing Key Issues

SESSION 5: Clinical, Social, and Policy Considerations

- Chairperson: D. Lowenstein, University of California, San Francisco
- A. Poduri, Boston Children's Hospital, Massachusetts: Precision medicine in the epilepsy clinic: Lessons from the early days.
- T. Dixon-Salazar, Citizens United for Research in Epilepsy, Chicago, Illinois: Community support of precision medicine in epilepsy.
- V. Whittemore, National Institute of Neurological Disorders and Stroke, Bethesda, Maryland: Epilepsy within NIH precision medicine initiative.

General Discussion and Summary

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# Preventing Inherited BRCA Cancer: A Think Tank for Innovative Strategies, Milestone Objectives, and Research Priorities

# November 11-13

FUNDED BY	HeritX
ARRANGED BY	<ul> <li>A. Ashworth, University of California Cancer Center, San Francisco</li> <li>T. Bock, HeritX, Chester, New Jersey</li> <li>L. Brody, National Human Genome Research Institute, NIH, Bethesda, Maryland</li> </ul>

Twenty years ago, the discovery of the BRCA genes was heralded as the most exciting story in medical science. At Banbury in 1995, scientists optimistically predicted that this new genetic information would lead to new treatments within a decade. Yet while much knowledge has been gained about the clinical consequences and individual risk associated with BRCA mutations, the medical management of BRCA carriers is still limited. Families affected by a BRCA mutation urgently need a medical intervention that prevents all types of BRCA-related cancer and leaves people whole and healthy. This is the goal of the HeritX Foundation. As a first step, HeritX assembled experts across a wide range of topics to collectively design a research agenda with actionable short-term milestones toward the prevention of BRCA-related cancer.

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

**SESSION 1:** Defining the Goal of Preventing Inherited BRCA Cancer

The HeritX Global Research Initiative for Preventing Inherited Cancer T. Bock, HeritX, Chester, New Jersey

Chairperson: T. Bock, HeritX, Chester, New Jersey



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- A. Ashworth, University of California Cancer Center, San Francisco
- L. Brody, National Human Genome Research Institute, NIH, Bethesda, Maryland

### Integrated R&D Planning Leads to Faster Patient Benefit

D. Hager, HeritX, Chester, New Jersey

### **General Discussion**

### Eliminating the Needs of Affected Families

J. Morris, HeritX, Inc., Santa Monica, California (Facilitator) I. Bock, Chester, New Jersey P. Munster, University of California, San Francisco

M. Unger, Los Angeles, California

## Translating the Patient Goal into a Target Therapy Profile for Preventing Inherited BRCA Cancers

D. Hager, HeritX, Chester, New Jersey

**SESSION 2:** How Can We Accomplish a Prevention of All Types of Inherited BRCA Cancer?

Chairpersons: L. Brody, National Human Genome Research Institute, NIH, Bethesda, Maryland, and T. Bock, HeritX, Chester, New Jersey

BRCA Overview: The Genes, Proteins, and Their Cellular Roles

R. Scully, Beth Israel Deaconess Medical Center, Boston, Massachusetts

Tackling Seemingly Insurmountable Scientific Challenges: "Think Different!"

M. Olson, University of Washington, Seattle

### Discussion

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Breakout Group A:- Banbury Conference Room Facilitator: L. Brody, National Human Genome Research In-

stitute, Bethesda, Maryland

## Breakout Group B:- Meier House Library

Facilitator: W. Foulkes, Montreal General Hospital, Quebec, Canada

Breakout Summaries to the Whole Group: Banbury Conference Room

- SESSION 3: Overcoming Current Hurdles. The Biology of Risk: Identifying the First Steps of Cancer Development in Heterozygous BRCA Mutation Carriers for Therapeutic Targeting
- Chairpersons: B. Ponder, CRUK Cambridge Institute, United Kingdom, and A. Ashworth, University of California, San Francisco

### Research Strategies to Identify Early Steps in Pathogenesis

J. Brugge, Harvard Medical School, Boston, Massachusetts

### Discussion

- Technology to Pursue These Strategies in Healthy BRCA Carriers
- P. Spellman, Oregon Health & Science University, Portland, Oregon
- SESSION 4: Pre-empting Future Hurdles: Surrogate Endpoints—Developing Candidate Therapies Faster
- Chairpersons: J. Garber, Dana-Farber Cancer Institute, Boston, Massachusetts, and D. Parkinson, New Enterprise Associates, Palo Alto, California

Research Strategies: Identifying Biomarkers or Bio-Signatures That Could Become Surrogate Endpoints

S. Domchek, University of Pennsylvania, Philadelphia

Non-Cancer Manifestations in BRCA Carriers: Do They Exist? Are They Clinically Meaningful? How To Study?

J. Garber, Dana-Farber Cancer Institute, Boston, Massachusetts

SESSION 5: Implementing Banbury Outcomes after Banbury

- Chairperson: T. Bock, HeritX, Chester, New Jersey
- A. Ashworth, University of California Cancer Center, San Francisco
- L. Brody, National Human Genome Research Institute, Bethesda, Maryland

Conclusion of the Workshop

# How Can the Genetics and Neurobiology of Borderline Personality Disorder Contribute to Its Diagnosis and Treatment?

## November 15-18

FUNDED BY Oliver Grace Fund, Matthew Warren Fund for Mental Health; The Menninger Clinic; Mt. Sinai School of Medicine; NEA-BPD; and The Soref Family

ARRANGED BY J. Oldham, The Menninger Clinic, Houston, Texas A. New, Mount Sinai School of Medicine, New York

Borderline personality disorder (BPD) is a serious and disabling psychiatric disorder that is the most prevalent personality disorder in psychiatric treatment populations. Much is now known about the neurobiology and pathophysiology of BPD, and evidence-based treatment strategies have been demonstrated. A great deal of work remains to be done, however, to harness new strategies such as genomics and neuroimaging to identify BPD-specific neuropathology. Biomarkers are needed to facilitate early identification and prevention of BPD, and to monitor its course and treatment. This conference was intended to explore areas such as temperament, emotion regulation, developmental attachment and its disruptions, impulse control, and interpersonal functioning and to collectively design a new research agenda for BPD.



J. Oldham

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

Conference Introduction and Structure: J. Oldham, The Menninger Clinic, Houston, Texas A. New, Mount Sinai School of Medicine, New York



- SESSION 1: Phenomenology of Borderline Personality Disorder
- Chairperson: J. Oldham, The Menninger Clinic, Houston, Texas
- J. Oldham, The Menninger Clinic, Houston, Texas: Dimensional vs. categorical diagnosis of BPD and the alternative model.
- A. Skodol, University of Arizona College of Medicine, Phoenix: Back to the future: BPD Research Foundation Redux.
- M. Zanarini, McLean Hospital, Belmont, Massachusetts: The long-term course of BPD.
- P. Tyrer, Imperial College London, United Kingdom: How the new classifications of personality disorder might help the genetics and neurobiology of that very heterogeneous condition, borderline personality disorder.
- C. Sharp, University of Houston, Texas: The social-cognitive basis of BPD: A translational approach.

### Discussion and Summary

### **SESSION 2:** Family Perspective

- P. Hoffman, National Education Alliance for Borderline Personality Disorders, Mamaroneck, New York
- V. Porr, TARA Association for Borderline Personality Disorder, New York
- K. Warren, Acts of Mercy Foundation, Rancho Santa Marguerita, California

#### SESSION 3: Genetics of BPD

Chairperson: D. Goldman, National Institute on Alcohol Abuse & Alcoholism, Rockville, Maryland

- D. Goldman, National Institute on Alcohol Abuse & Alcoholism, Rockville, Maryland: Chemogenetics for addictions: Challenges and opportunities.
- M. Distel, GGZ in GeestIVU Medical Center, Amsterdam, The Netherlands: Genetics of BPD: What twin studies have learned us and what is left to learn.
- M. Perez-Rodriguez, Mount Sinai School of Medicine, New York: Current status of genetic research in borderline personality disorder.
- Sh. Purcell, Icahn School of Medicine at Mount Sinai, New York: Progress and prospects in neuropsychiatric genetics: Lessons learned from schizophrenia and other disorders.

### Session Discussion and Summary

#### **SESSION 4:** Brain Circuits

- Chairperson: A. New, Mount Sinai School of Medicine, New York
- A. New, Mount Sinai School of Medicine, New York: An illness of impaired emotional interoception.
- C. Schmahl, Central Institute of Mental Health, Mannheim, Germany: How neuroimaging can be used to improve psychotherapy for emotion dysregulation.

### Session Discussion and Summary

### SESSION 5: Animal Models

- Chairperson: J. Oldham, The Menninger Clinic, Houston, Texas
- M. Bohus, Central Institute of Mental Health, Mannheim, Germany: Toward an animal model for aspects of BPD: The peer group rejection paradigm in mice.



K. Warren, V. Porr



D. Goldman

S. Russo, Icahn School of Medicine at Mount Sinai, New York: Can we model axis II pathology in mice to identify circuit abnormalities?

Session Discussion and Summary

# SESSION 6: Treatment

- Chairperson: R. Kissell, University of California, Los Angeles, Semel Institute, Beverly Hills
- R. Kissell, University of California, Los Angeles, Semel Institute, Beverly Hills, California: Treatment for BPD: What we have and what we need.

- B. Stanley, Columbia University, New York: Mechanisms of action of treatment for BPD: What we know and what we don't know.
- M. Goodman, Bronx VA Medical Center, Bronx, New York: The neurobiology of DBT treatment response.

### Session Discussion and Summary

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SESSION 7: Wrap-up and Future Directions

Moderators: A. New, Mount Sinai School of Medicine, New York, and J. Oldham, The Menninger Clinic, Houston, Texas

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# Tumor Cell Metabolism: Finding New Targets for Therapeutic Intervention

## December 7–10

funded by	Oliver Grace Cancer Research Fund and OBX, Inc.
ARRANGED BY	L. Cantley, Weill Cornell Medical College, New York S. McKnight, University of Texas Southwestern Medical Center, Dallas

Recent research has provided many insights into the biochemical basis for alterations in the metabolic state of tumors compared to normal tissues. This growing body of knowledge about tumor metabolism has revealed new targets for pharmaceutical intervention, and several new experimental drugs that target metabolic enzymes have entered clinical trials. Participants reviewed new metabolic targets, discussed biomarkers that are likely to predict which tumors are likely to respond to drugs that hit these targets, examined potential mechanisms of resistance to such therapies, and discussed drug combinations that could prevent resistance.

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

Opening Remarks: J.D. Watson, Cold Spring Harbor Laboratory

# SESSION 1: Hypoxia

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- Chairperson: J.M. Bishop, University of California, San Francisco
- R. Bruick, University of Texas Southwestern Medical Center, Dallas: Regulation of hypoxia-inducible factor 2: Sensing opportunities.
- J. Josey, Peloton Therapeutics, Inc., Dallas, Texas: Modulation of hypoxia-inducible factor-2α.

W. Kaelin, Dana-Farber Cancer Institute, Cambridge, Massachusetts: New targets emerging from studies of VHL and IDH.





H. Varmus, M. Bishop, J. Witkowski

- SESSION 2: Addressing Cancer Metabolism in the Clinic
- Chairperson: J.M. Bishop, University of California, San Francisco
- R. DeBerardinis, University of Texas Southwestern Medical Center, Dallas: Metabolic heterogeneity in human lung tumors.
- M. Dorsch, Agios Pharmaceuticals, Cambridge, Massachusetts: Development of mutant IDH inhibitors from concept to clinic.
- E. Maher, University of Texas Southwestern Medical Center, Dallas: Metabolic reprogramming of bioenergetic substrate utilization: When does it occur?

SESSION 3: Signaling Pathways That Control Metabolism

Chairperson: H. Varmus, Weill Cornell Medical College, New York

- M. Brown, University of Texas Southwestern Medical Center, Dallas: Scap: Sterol sensor and SREBP regulator.
- B. Manning, Harvard University, Boston, Massachusetts: Oncogene control of lipid and nucleotide metabolism.
- J. Blenis, Weill Cornell Medical College, New York: New mechanisms for mTORC1-dependent regulation of cell metabolism.
- L. Cantley, Weill Cornell Medical College, New York: Managing ROS in cancer cells.
- A. Kimmelman, Dana-Farber Cancer Institute, Boston, Massachusetts: Identifying metabolic vulnerabilities in pancreatic cancer.
- T. Miller, IC MedTech Corp, El Cajon, California: Vitamin C selectively targets cancer cells: Can combining other redoxactive molecules and chemotherapy translate into safer, more effective, and more affordable clinical protocols?
- K.-L. Guan, University of California, San Diego: The Hippo pathway in cellular nutrient response.



K.-L. Guan, A. Levine, K. Vousden

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- R. Shaw, Salk Institute for Biological Studies, La Jolla, California: The LKB1–AMPK pathway: Metabolic rewiring and therapeutic targeting.
- Y.-S. Lee, Johns Hopkins University, Baltimore, Maryland: Structure and functional analysis of dimeric PKM2.
- H. Christofk, University of California, Los Angeles: Use of viruses to study cancer metabolism.
- R. Evans, Salk Institute for Biological Studies, La Jolla, California: Stromal regulation of pancreatic cancer epigenome and metabolome.

### General Discussion Highlighting Key Points

SESSION 4: Cellular Control by Metabolic Intermediates

Chairperson: A. Levine, Institute for Advanced Study, Princeton, New Jersey

- K. Vousden, Beatson Institute, Glasgow, United Kingdom: One carbon metabolism in cancer cells.
- B. Tu, University of Texas Southwestern Medical Center, Dallas: Intracellular pathways responsive to SAM.
- J. Rutter, University of Utah School of Medicine, Salt Lake City: The impact of pyruvate metabolism on stemness in normal and cancer settings.
- J. Locasale, Duke University, Durham, North Carolina; One carbon metabolism and epigenetics.
- S. Gross, Weill Cornell Medical College, New York: Untargeted stable isotope tracing to define the contribution of serine to folate-mediated 1-carbon trafficking.

### General Discussion Highlighting Key Points

#### **SESSION 5:** Alternative Nutrients for Cancer Cells

- Chairperson: A. Levine, Institute for Advanced Study, Princeton, New Jersey
- E. White, The Cancer Institute of New Jersey, New Brunswick: Autophagy and cancer metabolism.
- R. Abraham, Pfizer Worldwide Research & Development, San Diego, California: Interplay between glutamine meta-

bolism and autophagy during tumor cell growth and stress responses.

- L. Trotman, Cold Spring Harbor Laboratory: Mitochondria and dietary control of prostate cancer.
- G. Smolen, Agios Pharmaceuticals, Cambridge, Massachusetts: Differential aspartate usage identifies a subset of cancer cells particularly dependent on a novel metabolic target.

### SESSION 6: Review of Key Issues

Chairpersons: L. Cantley, Weill Cornell Medical College, New York, and S.L. McKnight, University of Texas Southwestern Medical Center, Dallas

### Closing Remarks:

J.D. Watson, Cold Spring Harbor Laboratory



H. Christofk, J. Watson

# **BANBURY CENTER GRANTS**

Grantor	Program	Duration of Grant	2015 Funding
FEDERAL SUPPORT			
National Institute of Mental Health National Institute of Mental Health	NIMH Brain Camp VII Brain Rhythms as Potential Targets for Intervention in Cognitive Dysfunctions	2015 2015	\$28,340 34,920
NONFEDERAL SUPPORT			
Alkermes, Inc.	Therapeutic Use of Ketamine for Treating Severe Depression: Risks and Potential	2015	6,000
ALS Association of Greater New York	Therapeutic Developments for ALS: Antisense, Therapy, and Stem Cells	2015	56,326
amfAR	HIV-1 and How to Kill a Killer: Attempts at Total or Functional Cure of HIV-1	2015	12,000
BBSRC, Genome Analysis Centre	Beyond the Wheat Genome	2015	18,693
Boehringer Ingelheim Fonds	Communicating Science	2015	64,852
Clarus Ventures	Scientific and Clinical Foundation for Precision Medicine in Epilepsy	2015	10,000
Cold Spring Harbor Laboratory Corporate Sponsor Program	Creating Patient-Specific Neural Cells for the In Vitro Study of Brain Disorders	2015	45,414
Cold Spring Harbor Laboratory Corporate Sponsor Program	What Is Needed to Harness Chemogenetics for the Treatment of Human Brain Disorders?	2015	37,736
Cold Spring Harbor Laboratory Corporate Sponsor Program	Therapeutic Approaches to Prion Disease and Other Neurodegenerative Conditions Associated with Protein	2015	34,738
Corporate opensor riegtam	Misfolding		
Columbia University Institute for Genomic Medicine	Scientific and Clinical Foundation for Precision Medicine in Epilepsy	2015	10,956
CURE Epilepsy	Scientific and Clinical Foundation for Precision Medicine in Epilepsy	2015	15,000
Eli Lilly and Company	Biophysical Properties and Biological Significance of Amyloid-B Assemblies	2015	10,000
Gilead Sciences, Inc.	HIV-1 and How to Kill a Killer: Attempts at Total or Functional Cure of HIV-1	2015	10,000
HeritX	Preventing Inherited BRCA Cancer: A Think Tank for Innovative Strategies, Milestone Objectives, and Research Priorities	2015	45,608
Janssen Research & Development	Therapeutic Use of Ketamine for Treating Severe	2015	25,000
Kyowa Hakko Kirin, Co. Ltd.	Biophysical Properties and Biological Significance of Amyloid-B Assemblies	2015	5,000
Lustgarten Foundation for Pancreatic	The Lustgarten Foundation Scientific Meeting	2015	30,267
The Margaret Clark Morgan Foundation	Thriving with Schizophrenia	2015	35,948
The Menninger Clinic	How Can the Genetics and Neurobiology of Borderline Personality Disorder Contribute to Its Diagnosis and Treatment?	2015	8,000
Mt. Sinai Medical School	How Can the Genetics and Neurobiology of Borderline Personality Disorder Contribute to Its Diagnosis and Treatment?	2015	2,000
NEA-BPD	How Can the Genetics and Neurobiology of Borderline Personality Disorder Contribute to Its Diagnosis and Treatment?	2015	1,500
Oliver Grace Cancer Fund	Mitochondria and Cancer	2015	50,626

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# BANBURY CENTER GRANTS (Continued)

Grantor	Program	Duration of Grant	2015 Funding
Oliver Grace Cancer Fund	Tumor Cell Metabolism: Finding New Targets for Therapeutic Intervention	2015	\$23,297
Oliver Grace Fund	Exercise Science and Health	2015	25,000
Oliver Grace Fund	How Can the Genetics and Neurobiology of Borderline Personality Disorder Contribute to Its Diagnosis and Treatment?	2015	15,000
OBX Inc.	Tumor Cell Metabolism: Finding New Targets for Therapeutic Intervention	2015	25,000
Pairnomix	Scientific and Clinical Foundation for Precision Medicine in Epilepsy	2015	10,300
The Soref Family	How Can the Genetics and Neurobiology of Borderline Personality Disorder Contribute to Its Diagnosis and Treatment?	2015	2,000
State of Maryland	HIV-1 and How to Kill a Killer: Attempts at Total or Functional Cure of HIV-1	2015	19,850
The Swartz Foundation	Neuronal Response Variability and Correlation	2015	46,544
University of California, San Francisco and The Ron and Sanne Higgins Epilepsy Research Fund	Scientific and Clinical Foundation for Precision Medicine in Epilepsy	2015	14,000
University of Maryland Baltimore Foundation	HIV-1 and How to Kill a Killer: Attempts at Total or Functional Cure of HIV-1	2015	4,091
University of Minnesota Grossman Center	Biophysical Properties and Biological Significance of Amyloid-β Assemblies	2015	26,487
Matthew Warren Fund for Mental Health	How Can the Genetics and Neurobiology of Borderline Personality Disorder Contribute to Its Diagnosis and Treatment?	2015	10,000

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Jan A. Witkowski, Executive Director Janice Tozzo, Executive Assistant Patricia Iannotti, Secretary Barbara Polakowski, Hostess Jose Pena Corvera, Supervisor, Grounds Fredy Vasquez, Groundskeeper Joseph McCoy, Groundskeeper

# Cold Spring Harbor Laboratory

Jamie C. Nicholls, Chairman Bruce Stillman, President & Chief Executive Officer W. Dillaway Ayres, Jr., Chief Operating Officer

Founded in 1890, Cold Spring Harbor Laboratory (CSHL) has shaped contemporary biomedical research and education with programs in cancer, neuroscience, plant biology, and quantitative biology. A 501(c)(3) nonprofit organization, CSHL is independently ranked in the top 1% of charities by Charity Navigator. For more information, visit www.cshl.edu.