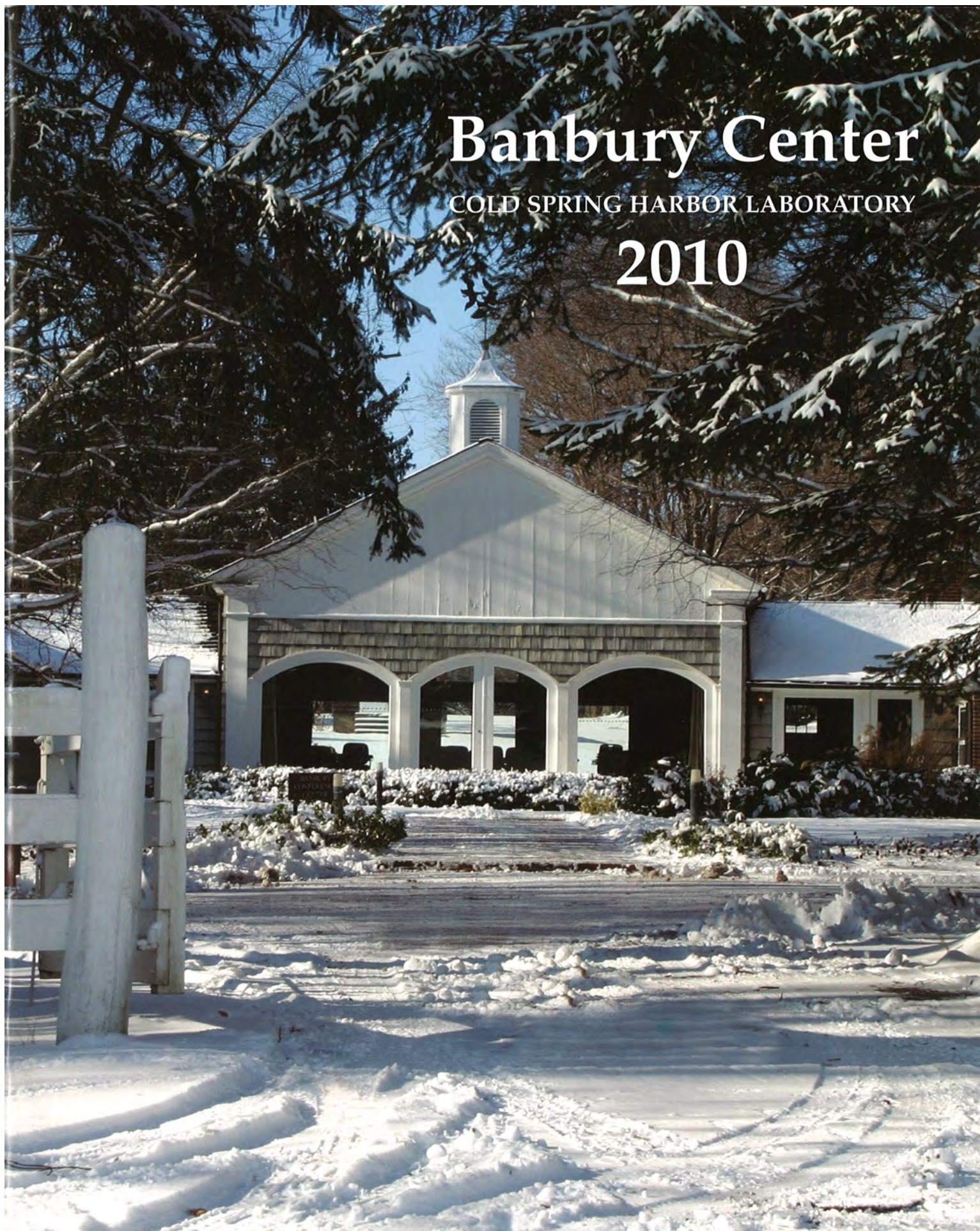


# Banbury Center

COLD SPRING HARBOR LABORATORY

## 2010





# BANBURY CENTER

## EXECUTIVE DIRECTOR'S REPORT

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The Banbury Center is now in its 33rd year and continues to be used intensively. In 2010, there were 22 science-related meetings attended by 577 participants. In addition, the Center was made available to community groups on five occasions. The Meetings and Courses Program held six lecture courses during the summer months and the Watson School of Biological Sciences used the Center for its two *Topics in Biology* courses.

Of the 577 participants, 486 (71%) were from the United States. They were drawn from 33 states, the geographical distribution reflecting the degree of biomedical research in the United States. The 91 foreign participants came from 18 countries, the majority from the United Kingdom. The ratio of male-to-female participants remains at 2:1.

The meeting topics were unusually wide-ranging, even for the Banbury Center. The Center has always held meetings on policy issues, issues where biomedical research is relevant to matters of societal interest. The first of two such meetings in 2010 concerned science and economic policy. The American Recovery and Reinvestment Act (ARRA) provided an extra \$10.4 billion funding over a 2-year period for the National Institutes of Health (NIH) to promote biomedical research through funding new projects, construction, and the purchase of equipment. However, although this has been a great success, the question arises as to what will happen when the ARRA funding comes to an end? *How Can We Maintain the Stability of Biomedical Research and Development at the End of the ARRA?* examined first, how NIH spent the ARRA funding and second, how can federal agencies, universities, research institutes, and individual investigators manage the ending of ARRA support. Participants included officials from NIH, universities, research institutes, economists, and scientists.



M. Battin, A. Asche, E. MacDonald

The second meeting, funded by the Ellison Medical Foundation, discussed *Easeful Death: 21st Century Perspectives on Assisted Suicide*. End-of-life issues involve profound legal, moral, religious, and biomedical questions and evoke intense passions. The Banbury Center is admirably suited to tackle difficult topics, although these are more usually controversies in the interpretation of scientific data. Discussions covered three broad areas. First, there was an extended discussion on whether there are distinctions to be drawn between a physician acquiescing to a patient's refusal of food and water, assisting in suicide by making it possible through providing materials, and the physician actively taking part in the suicide. Second, participants from Belgium and The Netherlands presented data on whether the legalization of euthanasia and assisted suicide changes the behaviors of patients and physicians, and whether the slippery slope argument carries any weight. Third, we discussed the changes in the political and legal apparatus that will have to come about before there can be acceptance of easeful death as a proper end to life. Participants included scientists, physicians, lawyers, philosophers, and religious leaders of differing opinions and although no consensus was likely to have been reached, the discussions were of remarkable quality and interest.

Turning to more typical Banbury Center topics, there were several meetings on cancer. *Energy Metabolism, the Cell Cycle, and Cancer* explored an old hypothesis on the fundamental nature of cancer in the light of modern molecular analysis. The Warburg Hypothesis was advanced by Otto Warburg in 1924 when he found that tumor cells mainly generate energy anaerobically by glycolysis

rather than by oxidative metabolism. Warburg believed that this was a fundamental characteristic of cancer cells, a thesis that fell out of fashion with the discovery of oncogenes and a focus on the genetic changes in cancer. However, in recent years links have been found between glycolysis and oncogenes and participants in this meeting reviewed these findings. For example, one session was devoted to cancer metabolism and the tumor suppressor protein p53.

A second meeting on cancer, *Tumor Microenvironment and Metastasis*, reviewed the evidence that the cancer cell is not a “renegade” cell, growing and multiplying without regard for its surroundings. On the contrary, there is increasing evidence that the behavior of a cancer cell, particularly metastasis, is influenced by its microenvironment, which includes other cells and the tumor-associated extracellular matrix. Participants examined such questions as, Is all the information needed for a cell to metastasize autonomous or does the tissue microenvironment have a role in determining this process? Does disrupting the tumor microenvironment have a positive or negative impact on metastatic potential of cancer cells? Can the microenvironment explain why many primary tumors favor secondary tumor formation in specific organs? The meeting explored what constitutes the tumor microenvironment and examined its functional impact on metastasis with specific focus on new targets for treatment of metastatic cancer.

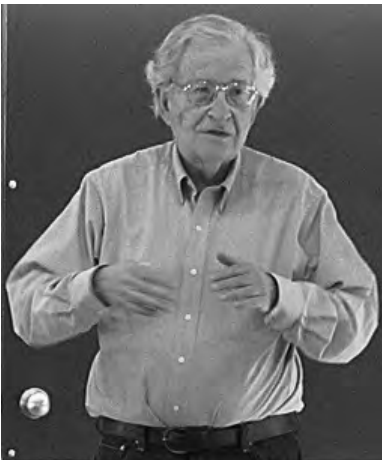
Banbury Center has a long-standing interest in promoting research on psychiatric disorders, beginning in the early 1990s when RFLP (restriction-fragment-length polymorphism) linkage mapping was being used to try to locate genes involved in schizophrenia and depression. These and later genetic mapping strategies such as genome-wide association studies have proved disappointing and thus, it was fascinating to hold a meeting—*The Lateral Habenula: Its Role in Behavior and Psychiatric Disorders*—based on a well-defined, if poorly understood, anatomical feature of the brain. The starting point for interest in the lateral habenula was the observation that deep-brain stimulation of the area in a woman profoundly disabled by depression led to a remission that persisted as long as the stimulation continued. This meeting began with the fundamental anatomy and functional connections of the habenula before progressing to its role in cognition and how it might have a role in clinical depression.

A closely related meeting was *Linguistic Phenotypes: Toward a Biological Understanding of Language*

that explored the thesis that language can provide a window into mental function which can be exploited for the study and understanding of neuropsychiatric disorders. If linguistic performance reflects thought processes, quantitative measures defined on the basis of linguistic performance might be useful in characterizing phenotypic variability among individuals. Specific examples include autism, specific language impairment, and Williams syndrome. Schizophrenia, which includes thought disorder in its symptom list, may also be amenable to useful linguistic phenotyping. Participants included linguists and psycholinguists interested in human neurobiology and disease, as well as biologists working on autism, schizophrenia, and other neuropsychiatric disorders. We were particularly pleased that Noam Chomsky took part in the meeting.

There were two Banbury Center meetings relating to history. Mutations are essential for genetic analysis and T.H. Morgan’s white-eyed *Drosophila* mutation initiated the modern era of genetics. Mutations cause inherited disorders and generate the variability on which natural selection acts. The first of our two historical meetings, *Mutagenesis: What It Means and How It Has Changed*, examined

how genes and mutations were regarded in the early days of genetics and how those ideas changed with the advent of molecular genetics in the 1950s and 1960s. There were also presentations on the consequences of environmental sources of mutation: radiation and chemical carcinogens. We also discussed contemporary research on mutations, such as copy-number variation, and mutation-like phenomena in prions.



N. Chomsky



N. Federoff, C. Weisman, E. Friedberg, S. Brenner, A. Creager

Lewis Lehrman (The Lehrman Institute) wishes to encourage the use of genetic and genomic analyses to inform our knowledge of history and has established a program to foster interactions between scientists and historians. Examples of the power of such interactions are evident in studies tracking the movements of early human beings out of Africa and subsequent spread of populations throughout the globe; where and how key events in domestication of plants and animals occurred; and what DNA sequencing is telling us about our relationship with Neanderthals. Participants in *DNA, Genetics, and the History of Mankind* reviewed these and other topics. The meeting closed with a free-ranging discussion on how to promote interactions between historians and scientists and on what topics should be covered in the follow-up meeting.

The Banbury Center could not operate at its high level without the hard work of many people. The Center is especially fortunate in having Janice Tozzo and Susanne Igneri ensuring that the meetings run smoothly, and Basia Polakowski making sure that participants are welcome in Robertson House. Sonny Leute, Alvin Watson, and Fredy Vasquez look after the grounds, dealing with vast amounts of leaves in the fall and, this year, vast amounts of snow in the winter. Jon Parsons is indefatigable in handling AV requirements and Connie Brukin took the photographs which enliven the report. Culinary Services feeds our participants and Housekeeping copes admirably with the rapid turnover of guests.

**Jan Witkowski**  
Executive Director

# BANBURY CENTER MEETINGS

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## p53 Retreat

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January 28–30

FUNDED BY      **Columbia University**, New York, New York

ARRANGED BY    **C. Prives**, Columbia University, New York, New York  
                      **S. Lowe**, Cold Spring Harbor Laboratory, New York

The p53 protein first identified in 1979 and believed to be an oncoprotein was shown in 1989 to be a tumor suppressor. It has a central role in cell cycle control, regulation of DNA repair, and the initiation of apoptosis and is the gene most frequently mutated in cancers. p53 was named the 1993 “Molecule of the Year” by *Science*. It is not surprising then that p53 has been the subject of intensive investigation, not least by research groups at Cold Spring Harbor (Lowe), Princeton (Levine), and Columbia (Prives and Cordon-Cardo). Members of these laboratories came to Banbury Center to report on their work and to promote interactions between the groups.

### Levine Lab Presentation #1

D. Carpizo: p53 allele-specific synthetic lethality.

### Cordon-Cardo Lab Presentation #1

O. Karni-Schmidt: New findings on p53 and its possible roles in bladder cancer and development.

### Prives Lab Presentation #1

S. Singer: Nup98, a potential tumor suppressor regulates select p53 target gene expression by a novel mechanism.

### Lowe Lab Presentation #1

C. Scuoppo: The polyamine–hypusine axis defines a tumor suppressor network in human lymphoma.

### PI PLANNING MEETING

### Cordon-Cardo Lab Presentation #2

A. Jia: microRNAs in bladder cancer progression.

### Levine Lab Presentation #2

H. Mizuno: Stem cell signatures in breast cancer with p53 mutations.

### Prives Lab Presentation #2

W. Freed-Pastor: Mutant p53 prevents formation of mammary acini in three-dimensional culture.

### Lowe Lab Presentation #2

L. Dow: How to make a hairy mouse: New transgenic shRNA technologies to allow reversible loss of function phenotypes in adult mice.

### Guest Lecturers

R. Parsons: PTEN regulation in cancer: What is the contribution of p53 mutation?

J. Manley: mRNA processing and cancer: Roles for p53 and other tumor suppressors and oncogenes.

### Prives Lab Presentation #3

C. Priest: A novel Mdm2 mutant that degrades itself preferentially over p53.

### Lowe Lab Presentation #3

Z. Zhao: p53 affects self-renewal in AML.

### Wrap-up Discussion

# The Lateral Habenula: Its Role in Behavior and Psychiatric Disorders

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February 28–March 3

FUNDED BY Marie Robertson Memorial Fund

ARRANGED BY F. Henn, Brookhaven National Laboratory, Upton, New York  
B. Li, Cold Spring Harbor Laboratory, New York

Depression is the disorder that is predicted to cause the greatest morbidity in the world by 2020, and a 2009 survey found 16% of Americans suffer from depression. Recently, deep-brain stimulation has been suggested as a possible therapy for this group, and data suggest that the target of this stimulation is the lateral habenula. This is a relatively little-studied part of the brain, and given these findings, this was the right time to critically review what is known of the function of this structure, its connections, and how they function. Participants included anatomists, physiologists, neuropharmacologists, and clinicians.

**Welcoming Remarks:** J. Witkowski, Banbury Center, Cold Spring Harbor Laboratory, New York  
**Background:** J. Watson, Cold Spring Harbor Laboratory, New York  
**Introduction:** F. Henn, Brookhaven National Laboratory, Upton, New York  
B. Li, Cold Spring Harbor Laboratory, New York

**SESSION 1:** The Lateral Habenula: Anatomical/Functional Connections and Cellular Biology  
**Chairperson:** O. Hikosaka, National Eye Institute, Bethesda, Maryland

M. Herkenham, National Institute of Mental Health, Bethesda, Maryland: The anatomical connections of the habenula nuclei, with a historical perspective.  
S. Sesack, University of Pittsburgh, Pennsylvania: Projections from the lateral habenula to midbrain dopamine neurons: indirect inhibitory control via the rostromedial mesopontine tegmentum.  
T. Jhou, National Institute on Drug Abuse, Baltimore, Maryland:

A convergence of aversion: Fear, disappointment, and inhibition in the rostromedial tegmentum (RMTg), a habenula target.

S. Haber, University of Rochester Medical Center, New York: The place of habenula in the reward circuit.

P. Shepard, University of Maryland, Baltimore: Stimulation of the lateral habenula inhibits the activity of midbrain dopamine neurons at the population level.





**SESSION 2: The Lateral Habenula: Anatomical/Functional Connections, and Cellular Biology (Cont'd)**

**Chairperson: S. Haber**, University of Rochester Medical Center, New York

- R. Veh, Charité—Universitätsmedizin Berlin, Germany:  
Intrinsic properties and connections of the lateral habenular complex in the rat.
- U. Kim, Pennsylvania State University College of Medicine, Hershey: Morphological and electrophysiological properties of the habenula.
- R. Blakely, Vanderbilt School of Medicine, Nashville, Tennessee: Ironing out a relationship between serotonin and

- the habenula: Insights from a genetic reference mouse population
- H. Okamoto, RIKEN Brain Science Institute, Wako City, Japan: Functional analysis of the dorsal habenula in zebra fish, an equivalent structure to the mammalian medial habenula.
- E. Turner, Seattle Children's Research Institute, Washington: A gene regulatory program for habenula development.

**SESSION 3: The Lateral Habenula and Cognitive Function**

**Chairperson: B. Moghaddam**, University of Pittsburgh, Pennsylvania

- O. Hikosaka, National Eye Institute, Bethesda, Maryland:  
Role of the lateral habenula in value-based decision-making.
- L. Lecourtier, Louis Pasteur University, Strasbourg, France:  
Role of the habenula in cognitive processes, linked to its regulatory role over many neurotransmitter systems.
- H. Piggins, University of Manchester, United Kingdom:  
Role of the habenula in the temporal regulation of brain states and behavior.

- M. Ullsperger, Radboud University Nijmegen, The Netherlands: Role of the habenula in performance monitoring and cognitive control. Approaches in human and animal research.
- G. Yadid, Bar-Ilan University, Ramat-Gan, Israel: Electrical stimulation of the lateral habenula for modulation of the reward system: Application to depression and addiction.

**SESSION 4: The Lateral Habenula and the Neural Mechanisms Underlying Clinical Depression**

**Chairperson: F.A. Henn**, Brookhaven National Laboratory, Upton, New York

- W. Drevets, University of Oklahoma-Tulsa University School of Community Medicine: Abnormalities of habenular structure and function in mood and anxiety disorders.
- J. Roiser, University College London, United Kingdom: Role of the habenula in psychiatric disorders.
- A. Sartorius, Central Institute of Mental Health, Mannheim,

- Germany: Lateral habenula and treatment-resistant depression: Results of functional inhibition of the lateral habenula in congenitally helpless rats and in a first patient.
- G. Northoff, University of Ottawa, Ontario, Canada: Subcortical regions and their relevance in emotion processing in depression.

**SESSION 5: The Lateral Habenula and Animal Models of Psychiatric Disorders**

**Chairperson: R. Dolan**, University College London, United Kingdom

- F. Henn, Brookhaven National Laboratory, Upton, New York:  
An animal model of depression: A key to understanding the road to the habenula.
- B. Li, Cold Spring Harbor Laboratory, New York: The synaptic circuitry of lateral habenula and learned helplessness.

- R. Malinow, University of California, San Diego: The synaptic and cellular changes in the lateral habenula of learned helplessness in rats.
- G. Goelman, Hadassah Hebrew University Medical Center, Jerusalem, Israel: Role of the habenula in depression that accompanies Parkinson's disease.



J. Watson, R. Malinow



B. Li, S. Sesack

# Epigenetic Reprogramming and Transgenerational Inheritance

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March 7–10

FUNDED BY            The Cold Spring Harbor Laboratory Corporate Sponsor Program

ARRANGED BY        R. Martienssen, Cold Spring Harbor Laboratory, New York  
                              W. Reik, Babraham Institute, Cambridge, United Kingdom

It is becoming clear that in mammals, plants, and other organisms, epigenetic mechanisms interface with genetic ones in regulating developmental decisions and pathways. Epigenetic reprogramming in the germ line and in early embryos allows pluripotency and stem cell plasticity, whereas the restriction of developmental plasticity also involves epigenetic mechanisms. Erasure of epigenetic marks in the germ line may be incomplete leading to epigenetic inheritance of altered developmental potential across generations. In plants, there is growing evidence for a parallel reprogramming event in both the male and the female germ lines. In pollen, this results in transposon activation followed by small RNA production and transport into gametes. This represents a mechanism for reinforcement of transposon control in each generation.

Welcoming Remarks: J. Witkowski, Banbury Center, Cold Spring Harbor Laboratory, New York  
Introductory Remarks: W. Reik, Babraham Institute, Cambridge, United Kingdom

## SESSION 1: Developmental Decisions

Chairperson: M.A. Surani, University of Cambridge, United Kingdom

T. Hiiragi, Max-Planck Institut für Molekulare Biomedizin,  
Muenster, Germany: Stochastic patterning in the development  
of pluripotency in mouse embryo.

M.-E. Torres-Padilla, Institut de Génétique et de Biologie,  
Strasbourg, France: Histone variants establish specialized  
chromatin signatures during reprogramming.

K. Hochedlinger, Harvard Stem Cell Institute, Cambridge,  
Massachusetts: Epigenetic similarities and differences between  
ES cells and iPS cells.

E. Heard, Institut Curie, Paris, France: Lessons from in vivo studies on  
X-chromosome inactivation and reactivation in different animals.

H. Blau, Stanford University School of Medicine, California: Role  
of active DNA demethylation by AID in reprogramming toward  
pluripotency.

P. Avner, Institut Pasteur, Paris, France: Developmental regulation  
of X-chromosome inactivation.





**SESSION 2: Reprogramming and Reproduction**

**Chairperson:** E. Heard, Institut Curie, Paris, France

- R. Martienssen, Cold Spring Harbor Laboratory, New York: Heterochromatin reprogramming and small RNA silencing in plant germ cells.  
 F. Berger, National University of Singapore: Reprogramming histone modifications in *Arabidopsis*.  
 J. Walter, Saarland University, Saarbrücken, Germany: Epigenetic reprogramming in the mouse zygote: Lessons from bisulphate sequencing.

- M. Surani, University of Cambridge, United Kingdom: Resetting the epigenome in embryos and germ line in the mouse.  
 R. Fischer, University of California, Berkeley: Reprogramming the endosperm genome.  
 W. Reik, Babraham Institute, Cambridge, United Kingdom: Reprogramming and programming of DNA methylation patterns in the genome.

**SESSION 3: Imprints and Inheritance**

**Chairperson:** T. Bestor, Columbia University, New York, New York

- H. Sasaki, Medical Institute of Bioregulation, Kyushu, Fukuoka, Japan: Role of the PIWI pathway in DNA methylation of the imprinted *Rasgrf1* locus in the male mouse germline.  
 A. Ferguson-Smith, University of Cambridge, United Kingdom: Genomic imprinting and the stability of the epigenetic program in developmental processes.  
 V. Colot, Ecole Normale Supérieure, Paris, France: Transgenerational inheritance of epigenetic variation in *Arabidopsis*: Mechanisms and phenotypic impact.

- D. Bourc'his, Institut Curie, Paris, France: Dnmt3L-independent way to methylate mammalian genomes.  
 W. Kelly, Emory University, Atlanta, Georgia: Epigenetic inheritance and reprogramming through the germline in *C. elegans*.  
 J. Paszkowski, University of Geneva, Switzerland: Stability of transgenerational epigenetic inheritance.

**SESSION 4: Environmental Effects and Evolution**

**Chairperson:** J. Rafalski, Dupont Experimental Station, Wilmington, Delaware

- N. Heintz, The Rockefeller University, New York, New York: The significance of 5-hydroxymethylcytosine in neuronal function.  
 A. Rao, Harvard Medical School, Boston, Massachusetts: Biological functions of TET proteins, enzymes that convert 5 methylcytosine to hydroxymethylcytosine DNA.  
 D. Ruden, Wayne State University, Detroit, Michigan: Epigenomic reprogramming of aggression in killer bees.

- J. Finnegan, CSIRO, Black Mountain, Australia: Flicking the switch on polycomb-regulated genes.  
 B. Hohn, Friedrich Miescher Institute of Biomedical Research, Basel, Switzerland: Environmental influences on plant genome dynamics.  
 U. Grossniklaus, Institute of Plant Biology, University of Zurich, Switzerland: Role of epigenetic regulation in evolution: The control of pollination syndromes.

**SESSION 5: Methylation Mechanisms**

**Chairperson:** H. Sasaki, Medical Institute of Bioregulation, Kyushu, Higashiaku, Japan

- T. Bestor, Columbia University, New York, New York: How much tissue-specific DNA methylation, and how important?  
 Y. Zhang, HHMI, University of North Carolina, Chapel Hill: Could the DNA demethylase please stand up?  
 S. Jacobsen, University of California, Los Angeles: DNA methylation in *Arabidopsis*.

**General Discussion:** W. Reik, Babraham Institute, Cambridge, United Kingdom

**Concluding Remarks:** R. Martienssen, Cold Spring Harbor Laboratory, New York



H. Blau, Y. Lazebnik

# The Second NIMH-Sponsored Brain Camp

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March 13–16

FUNDED BY                **National Institute of Mental Health**

ARRANGED BY        **M. Akil**, National Institute of Mental Health, Bethesda, Maryland  
                              **T. Insel**, National Institute of Mental Health, Bethesda, Maryland

We were very happy that the NIMH Brain Camp returned to Banbury in 2010 after its successful inauguration in 2009. 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 contributed to the meeting. The outcome of the meeting will be the start of a neuroscience curriculum that can eventually be shared with psychiatry training programs around the country.

**Introduction and Charge:** **M. Akil**, National Institute of Mental Health, Bethesda, Maryland  
**Rethinking Mental Illness:** **T. Insel**, National Institute of Mental Health, Bethesda, Maryland

**SESSION 1:** Circuitry Underlying Aggression/Circuitry of Emotional Learning  
**R. Yuste**, Columbia University, New York, New York  
**D. Salzman**, Columbia University, New York, New York

**SESSION 2:** How Circuits Develop  
**C. Nelson**, Harvard University, Boston, Massachusetts  
**B.J. Casey**, Cornell University, Ithaca, New York

**Discussion with the Organizers:** Teaching neuroscience in medical school and during psychiatry training: What's missing?

**SESSION 3:** Stress from Molecules to Circuits  
**H. Akil**, University of Michigan, Ann Arbor

**SESSION 4:** Circuitry Underlying Fear, Anxiety, and Recovery  
**J. LeDoux**, New York University, New York, New York  
**E. Phelps**, New York University, New York, New York

**Round Table Discussion with All Speakers**

**SESSION 5:** Translation: From Neurobiology to Treatments  
**K. Berman**, National Institute of Mental Health, Bethesda, Maryland  
**M. Bear**, Massachusetts Institute of Technology, Cambridge



# How Can We Maintain the Stability of Biomedical Research and Development at the End of the ARRA?

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April 25–27

FUNDED BY

Howard Hughes Medical Institute  
Alfred P. Sloan Foundation

ARRANGED BY

R. Freeman, NBER Science and Engineering Workforce Project, Harvard University, Cambridge, Massachusetts  
P. Stephan, Andrew Young School of Policy Studies, Georgia State University, Atlanta  
A. Wang, NBER Science and Engineering Workforce Project, Harvard University, Cambridge, Massachusetts  
J. Witkowski, Banbury Center, Cold Spring Harbor Laboratory, New York

The American Recovery and Reinvestment Act (ARRA) has provided an extraordinary \$8.2 billion in extramural funding to the National Institutes of Health and \$3 billion to the National Science Foundation as well as sizable funds to other agencies. These funds have been used to promote research, construct and renovate buildings and facilities, and purchase shared instrumentation. Biomedical research has benefited greatly from the ARRA, but there are increasing concerns about what will happen when the program comes to an end. It is important that the young researchers whose careers have been promoted through the support of the stimulus funds are not abandoned and that promising projects initiated using ARRA funds are not delayed. This workshop was held to discuss ways in which the government, universities, and other groups can “smooth” spending over time and find other ways to avoid problems.

Welcoming Remarks:

J. Witkowski, Banbury Center, Cold Spring Harbor Laboratory, New York

Introduction:

ARRA and NIH, and Government Support for Science

R. Freeman and A. Wang, NBER Science and Engineering Workforce Project, Harvard University, Cambridge, Massachusetts





**SESSION 1: How NIH Spent the ARRA Funding and Thoughts About Post-ARRA**

*Points to Consider*

L. Tabak, National Institute of Dental and Craniofacial Research, Bethesda, Maryland  
J. Niederhuber, National Cancer Institute, Bethesda, Maryland  
P. Stephan, Andrew Young School of Policy Studies, Georgia State University, Atlanta

**SESSION 2: What Is the Hard-Landing Scenario for Research Careers? What Is the Best-Case Scenario?**

*Points to Consider*

M. Teitelbaum, The Alfred P. Sloan Foundation, New York, New York  
J. Wiest, National Cancer Institute, Bethesda, Maryland  
H. Garrison, Federation of American Societies for Experimental Biology, Bethesda, Maryland

**SESSION 3: How Can Federal Agencies Manage the End of ARRA?**

*Points to Consider*

S. Turner, University of Virginia, Charlottesville  
J. McGowan, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland  
D. Mowery, University of California, Berkeley

**SESSION 4: How Can Universities and Research Institutes Manage the End of ARRA?**

*Points to Consider*

D. Korn, Harvard University, Cambridge, Massachusetts  
B. Stillman, Cold Spring Harbor Laboratory, New York

**SESSION 5: How Can PIs Manage the End of ARRA?**

*Points to Consider*

G. Marschke, National Bureau of Economic Research, Cambridge, Massachusetts  
R. Kolter, Harvard Medical School, Boston, Massachusetts  
M. Carlson, Howard Hughes Medical Institute, Chevy Chase, Maryland  
F. Murray, MIT Sloan School, Cambridge, Massachusetts

**SESSION 6: Innovative Approaches to Managing Support for Science**

*Points to Consider*

W. Goldschmidts, Cold Spring Harbor Laboratory, New York  
D. Goroff, The Alfred P. Sloan Foundation, New York, New York  
W. Schaffer, National Institutes of Health, Bethesda, Maryland

**Summary and Concluding Remarks**

R. Freeman, NBER Science and Engineering Workforce Project, Harvard University, Cambridge, Massachusetts



W. Schaffer



G. Marschke, P. Stephan



R. Freeman

# Linguistic Phenotypes: Toward a Biological Understanding of Language

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May 2–5

FUNDED BY      The Simons Foundation  
                     Université de Québec à Montréal  
                     Oliver Grace Fund

ARRANGED BY    R. Berwick, Massachusetts Institute of Technology, Cambridge  
                     N. Chomsky, Massachusetts Institute of Technology, Cambridge  
                     A. Di Sciullo, Université de Québec, Montréal, Canada  
                     P. Mitra, Cold Spring Harbor Laboratory, New York  
                     K. Wexler, Massachusetts Institute of Technology, Cambridge

The general idea of this meeting was that language provides a window into mental function that can be exploited for the study and understanding of neuropsychiatric disorders. One of the outstanding problems in the study of neuropsychiatric disorders is the relative paucity of objectively defined phenotypic measures, which can be used for diagnoses and in psychiatric genetic studies. Linguistic performance reflects thought processes, so the hypothesis is that quantitative measures defined on the basis of linguistic performance could be used to characterize phenotypic variability among individuals. Autism (which includes communication disorders), specific language impairment, as well as Williams syndrome (where language seems to be a relative strength) are of particular interest in this regard. Schizophrenia (which includes thought disorder in its symptom list) may also be amenable to useful linguistic phenotyping. Participants included linguists and psycholinguists interested in human neurobiology and disease, as well as biologists working on autism, schizophrenia, and other neuropsychiatric disorders.

A major goal of the meeting was to bring together scientists who are doing linguistic phenotyping with experts in the syndromes and geneticists, in an attempt to push along what we hope will be an exciting field that can make major contributions to one of the most important scientific (theoretical and applied) topics concerning humans.



**Introductory Remarks:** J. Witkowski, Banbury Center, Cold Spring Harbor Laboratory, New York

## INTRODUCTORY SESSION

**Chairperson:** R. Berwick, Massachusetts Institute of Technology, Cambridge

- P. Mitra, Cold Spring Harbor Laboratory, New York: Introduction.  
N. Chomsky, Massachusetts Institute of Technology, Cambridge: Language as a biological organ: What is it? How does it develop? And why?  
K. Wexler, Massachusetts Institute of Technology, Cambridge: Optional infinitives: A worked-out model of a particular linguistic characterization/phenotype.  
S. Fisher, University of Oxford, United Kingdom: Building bridges between genes, brains, and language.  
A. Monaco, Wellcome Trust Centre for Human Genetics, Oxford, United Kingdom: Genetics of specific language impairment.

## SESSION 1

**Chairperson:** A.-M. Di Sciullo, Université du Québec à Montréal, Canada

- N. Modyanova and K. Wexler, Massachusetts Institute of Technology, Cambridge: Linguistic phenotypes of more complex syntax: Phases and determiners in SLI, Williams syndrome, and autism.  
A. Perovic, University College London, United Kingdom: Grammatical impairments in autism spectrum, Williams syndrome, and Down syndrome.  
L. Kovelman, University of Michigan, Ann Arbor: Optional infinitive: Evidence of how adult brain processes grammatical errors that are typical.

## SESSION 2:

**Chairperson:** K. Wexler, Massachusetts Institute of Technology, Cambridge, Massachusetts

- L.-A. Petitto, University of Toronto, Canada: The phonetic, genetic, and brain-based changes that give rise to early language acquisition. Genes, brains, and cognition: space and language in Williams syndrome.  
M.-T. Guasti, University of Milan-Biocca, Milan, Italy: SLI and dyslexia: Differences between linguistic disorders in children.  
**General Discussion**  
B. Landau, Johns Hopkins University School of Medicine, Baltimore, Maryland  
K. Wexler, Massachusetts Institute of Technology, Cambridge  
P. Mitra, Cold Spring Harbor Laboratory, New York  
**Moderated Discussion:** White Paper

## SESSION 3

**Chairperson:** P. Mitra, Cold Spring Harbor Laboratory, New York

- D. Kimbrough Oller, University of Memphis, Tennessee and P. Niyogi, University of Chicago, Illinois: Vocal development theory and the automated identification disorders including autism.  
P. Suppes, Stanford University, California: Brain representations of linguistic constituents.  
P. Freed, Columbia University, New York, New York: Applications to clinical psychiatric practice.  
N. Schiff, Weill Cornell Medical College, New York, New York: Recovery of consciousness after severe brain injury. Opportunities for linguistics to inform research.  
D. Fox, Massachusetts Institute of Technology, Cambridge: Logic, language, and modularity.

## SESSION 4

**Chairperson:** N. Modyanova, Massachusetts Institute of Technology, Cambridge

- L. Osborne, University of Toronto, Canada: Duplication of genes on human chromosome 7q11.23 and their role in speech and expressive language.  
C. Mervis, University of Louisville, Kentucky: Speech and language abilities of individuals with Williams syndrome.  
S. Desiderio, Johns Hopkins School of Medicine, Baltimore, Maryland: TFII-I, a target of genetic lesions associated with the Williams–Beuren cognitive profile.  
W. McCombie, Cold Spring Harbor Laboratory, New York: Genetics becomes genomics.

**Discussion:** Future Planning



# Tumor Microenvironment and Metastasis

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May 5–7

FUNDED BY **Champalimaud Foundation and the Champalimaud Metastasis Programme**

ARRANGED BY **R. Kalluri**, Harvard Medical School, Boston, Massachusetts  
**J. Massague**, Memorial Sloan-Kettering Cancer Center, New York, New York

Approximately 80% of deaths related to cancer are associated with metastasis, and the central unanswered question remains the mechanism behind the systemic spread of cancer and secondary tumor formation in distant organs. It is clear that the microenvironment of a cancer cell has a key role in influencing its behavior and that this environment includes other cells and the tumor-associated extracellular matrix. The question, then, is what role does the tumor microenvironment have in metastasis? Is all the information needed for a cell to metastasize cell-autonomous or does the tissue microenvironment have a role in determining this process? Does disrupting the tumor microenvironment have a positive or negative impact on metastatic potential of cancer cells? Can the microenvironment explain why many primary tumors favor secondary tumor formation in specific organs? The meeting explored what constitutes the tumor microenvironment and examined its functional impact on metastasis with specific focus on new targets for treatment of metastatic cancer.

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

**Introductory Remarks:** J. Watson, Cold Spring Harbor Laboratory, New York

## SESSION 1

**Chairperson:** R. Kalluri, Harvard Medical School, Boston, Massachusetts:

J. Massague, Memorial Sloan-Kettering Cancer Center, New York, New York: Surviving the microenvironment.

Z. Werb, University of California, San Francisco: Transcriptional regulation of metastasis.



## SESSION 2

**Chairperson:** Z. Werb, University of California, San Francisco

- H. Dvorak, Beth Israel Deaconess Medical Center, Boston  
Massachusetts: Angiogenesis: The wrong therapeutic target?  
D. McDonald, University of California, San Francisco:  
Angiogenesis inhibitors: Risk and return.  
A. Harris, The Weatherall Institute of Molecular Medicine,

- Oxford, United Kingdom: Role of notch signaling and anti-VEGF therapy resistance.  
H. Hurwitz, Duke University Medical Center, Durham, North Carolina: Anti-angiogenesis therapy for cancer-expected and unexpected outcomes.

## SESSION 3

**Chairperson:** K. Cichowski, Brigham & Women's Hospital, Boston, Massachusetts

- M. Clarke, Stanford University, Palo Alto, California: Regulation of self-renewal by the microenvironment in normal epithelial stem cells and epithelial cancer cells or stem cells and cancer, two faces.  
R. Bjerkvig, University of Bergen, Norway: Cancer stem cells: Can they be defined?

- S. Haggarty, Massachusetts General Hospital, Boston: Patient-specific stem cell modes for characterizing disease and therapeutic discovery.  
J. Chang, Baylor College of Medicine, Houston, Texas: Multi-targeting of key self-renewal pathways.

## SESSION 4

**Chairperson:** J. Massague, Memorial Sloan-Kettering Cancer Center, New York, New York

- R. Kalluri, Harvard Medical School, Boston, Massachusetts: Pericyte coverage of tumor vessels: An adaptive host response to control tumor hypoxia?  
J. Sleeman, University of Heidelberg, Germany: The significance of lymphatic dissemination for metastasis: Blind alley, highway, or beacon?  
K. Cichowski, Brigham & Women's Hospital, Boston,

- Massachusetts: The inflammation, the microenvironment, and prostate cancer metastasis.  
D. Cheresh, University of California, San Diego, La Jolla: microRNA-132 mediated loss of p120RasGAP activates quiescent endothelium to facilitate pathological angiogenesis and tumor growth.

## SESSION 5

**Chairperson:** S. Mohla, National Cancer Institute, Bethesda, Maryland

- S. Rafii, Weill Cornell Medical Center, New York, New York: Contribution of the activated vascular niche to tumor growth.  
D. Lyden, Weill Cornell Medical Center, New York, New York:

- Early cellular molecular events for the information of metastatic niche.  
R. Hynes, Massachusetts Institute of Technology, Cambridge: Extracellular matrices of tumors.

## SESSION 6

**Chairperson:** Y. Kang, Princeton University, New Jersey

- S. Dias, Portuguese Institute of Oncology, Lisbon, Portugal: Metabolism and metastasis.  
S. Muthuswamy, Ontario Cancer Institute, University of Toronto, Canada: Cell polarity and cancer progression.  
O. Casanovas, Catalan Institute of Oncology, Barcelona, Spain:

- Tumor-adaptive responses to antiangiogenic therapies.  
E. Sahai, Cancer Research UK, London, United Kingdom: Cancer cell invasion in a complex environment.  
R. Sordella, Cold Spring Harbor Laboratory, New York: Intrinsic and extrinsic regulation of metastatic spread of NSCLC.

## SESSION 7

**Chairperson:** D. Lyden, Weill Cornell Medical College, New York

- M. Skobe, Mount Sinai School of Medicine, New York, New York: Role of lymphangiogenesis in tumor metastasis.  
J. Condeelis, Albert Einstein College of Medicine, Bronx, New York: Imaging of the tumor microenvironment of metastasis and the cell types within.

- Y. Kang, Princeton University, New Jersey: Tumor-stromal interactions in bone metastasis: Novel targets for therapeutic invention.

# Genetic Variation at a Single Locus for Prediction and Prevention of Late-Onset Alzheimer's Disease

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May 9–10

FUNDED BY            United Biomedical, Inc.

ARRANGED BY        C. Finstad, United Biomedical, Inc., Hauppauge, New York  
C. Wang, United Biomedical, Inc., Hauppauge, New York

Heterogeneity of response of individuals selected for clinical trials is a serious problem. Participants in this workshop explored ways to incorporate “pharmacogenetics” as a tool in the selection of individuals with pre-Alzheimer's disease for anti-A $\beta$  peptide immunotherapy. There was also discussion of how sequence variation is used to develop genome-wide association maps for determining how genomes are organized and regulated and their role in disease.

Opening Remarks:    J. Watson, Cold Spring Harbor Laboratory, New York  
C. Wang, United Biomedical, Inc., Hauppauge, New York

## SESSION 1: Genetic Variation and Early Detection of Alzheimer's Disease

A. Roses, Deane Drug Discovery Institute, Duke University and  
Cabernet Pharmaceuticals, Durham, North Carolina: Tomm40  
variable-length polymorphism predicts the age of late-onset

Alzheimer's disease (LOAD).  
T. Gingeras, Cold Spring Harbor Laboratory, New York: Origin  
of phenotypes: Genes and transcripts.





**SESSION 2: Immunotherapy and Immunoprevention of Alzheimer's Disease**

- M. Weksler, Weill Cornell Medical College, New York, New York:  
Role of a segmental immunodeficiency in age-associated and trisomy 21-associated dementia: From immunotherapy to immunoprevention.
- N. Relkin, Weill Cornell Medical College, New York, New York:  
Brain-imaging studies used in a phase II clinical study of intravenous immunoglobulin (IVIg) in patients with Alzheimer's disease.
- P. Szabo, Weill Cornell Medical College, New York, New York:

Amyloid- $\beta$  peptide targets for immunotherapy of Alzheimer's disease.

C. Finstad, A. Walfeld, F. Lin, K. Zhao, M.-J. Liao, C. Hung, C. Wang, United Biomedical, Inc., Hauppauge, New York and S. Lynn, B. Kuo, S.-N. Hsu, United Biomedical, Inc., Asia, Taiwan, Republic of China: Active immunization with UBITH® amyloid- $\beta$ 1-14 synthetic peptide vaccine (UB311): Design, development, and phase I clinical study.

**SESSION 3: Discussion and Summary**

- A. Roses, D. Crenshaw, D. Burns, Duke University School of Medicine, Durham, North Carolina and I. Grossman, T.W. Swanson, Cabernet Pharmaceuticals, Durham, North Carolina:  
Use of "Pharmacogenetics" in study design as a tool to maximize

the benefit/risk profile of a compound in development, particularly at "proof of concept." Suitable biomarkers for early detection of Alzheimer's disease and clinical trial design.

**Discussion Topics**

- Phase II clinical trial protocol for UBITH® A $\beta$ 1-14 vaccine (UB311) in individuals with mild Alzheimer's disease
- Phase II clinical trial protocol for UBITH® A $\beta$ 1-14 vaccine (UB311) in individuals with mild cognitive impairment (MCI) selected through MCI enrichment screening (amnesia testing and FDG-PET scan) with posthoc genotyping of APOE and 523 locus in TOMM40
- Retrospective genotyping of APOE and 523 locus in TOMM40 in normal and individuals with Alzheimer's disease in a Chinese population
- Experience with FDG-PET and PiB-PET for early diagnosis of individuals with pre-Alzheimer's disease



Robertson House patio

# Mutagenesis: What It Means and How It Has Changed

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May 15–18

FUNDED BY            Oliver Grace Cancer Fund

ARRANGED BY        J. Drake, National Institute of Environmental Health, Research Triangle Park, North Carolina  
J. Witkowski, Banbury Center, Cold Spring Harbor Laboratory, New York

Mutation is, of course, an integral part of genetics, although what are considered mutations has changed over the years as new techniques have led to new knowledge, leading to revisions of what “mutation” encompasses. This discussion meeting reviewed the developing concepts of mutation and understanding of the varied forms of mutation from the early days of *Drosophila* genetics to the present. Although the theme of the meeting was the history of the concept of mutation, contemporary research was also included, for example, on copy-number variation.

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

Introductory Remarks: J. Watson, Cold Spring Harbor Laboratory, New York

## SESSION 1

S. Mueller-Wille, University of Exeter, United Kingdom: The taxonomic roots of mutation: Constant varieties, sports, and pure lines.

E. Carlson, Bloomington, Indiana: Mutation and the gene in H.J. Muller's course, career, and influence.

S. Brenner, Salk Institute for Biological Studies, San Diego, California: Discovery of frame-shift mutants.

R. Falk, Hebrew University of Jerusalem, Israel: Mutagenesis as a genetic research strategy.

L. Campos, Drew University, Madison, New Jersey: From experimental evolution to genetic engineering: Mutation at Cold Spring Harbor Laboratory.

W. Maas, New York University School of Medicine, New York, New York: Role of serendipitous mutants in the elucidation of gene action and its regulation.

**Who Are They?** Identifying Participants in the Cold Spring Harbor Laboratory Symposia Photographs



## SESSION 2

- B. Bridges, Romsey, United Kingdom: From phenomenology to molecular understanding: Early work with ionizing radiation mutation.
- A. Creager, Princeton University, New Jersey: Mutation in the atomic age.
- B. Ames, Children's Hospital Oakland Research Institute, California: Mutation, detecting mutagens, and cancer prevention.
- J. Drake, National Institute of Environmental Health, Research Triangle Park, North Carolina: Artifacts of mutation ascertainment.
- J. Witkowski, Banbury Center, Cold Spring Harbor Laboratory, New York: Cold Spring Harbor Laboratory's contribution to the Human Genome Project.
- L. Pollock, Cold Spring Harbor Laboratory, New York: International data repository for the history of the Human Genome Project.
- B. Ames, Children's Hospital Oakland Research Institute, California: Delaying cancer and other age-related diseases with micronutrients.
- N. Fedoroff, U.S. Department of State, Washington, D.C.: McClintock, mutations, and epimutations.
- E. Friedberg, University of Texas Southwestern Medical School, Dallas: The molecular mechanism of DNA-damage-induced mutagenesis: After the SOS phenomenon to the present.
- Who Are They?** Identifying Participants in the Cold Spring Harbor Laboratory Symposia Photographs

## SESSION 3

- P. Hanawalt, Stanford University, California: Role of transcription in mutagenesis and genomic stability.
- M. Lynch, Indiana University, Bloomington: Evolution of the mutation rate.
- G. Montgomery, New York, New York: Changing views on sequence and synthesis.
- G. Walker, Massachusetts Institute of Technology, Cambridge: Positively-acting functions required for mutagenesis: Function and control of translesion DNA polymerases.
- C. Weissmann, Scripps Research Institute, Jupiter, Florida: Mutation-like events during prion propagation.



W. Maas, R. Maas, B. Ames



S. Brenner, J. Witkowski



E. Friedberg, E. Witkin

# PopTech Science and Public Leadership Fellows Retreat

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August 11–15

FUNDED BY            PopTech Accelerator

ARRANGED BY        L. Filderman, PopTech, Camden, Maine  
                              O. Wilder, PopTech, Camden, Maine

The PopTech Science and Public Leadership Fellows Program aims to develop a corps of extremely high potential, socially engaged working scientists who embody science as an essential way of thinking, discovering, understanding, and deciding, and who can communicate both their work and the importance of their fields to the public at large. The program gives these scientists intensive, high-quality training, a powerful social network, ongoing mentoring, and opportunities for public leadership and engagement. The Banbury Center was delighted to host the Fellows for the first meeting of the science and public leadership group.

**Welcome and Introductions:**    J. Witkowski, Executive Director, Banbury Center, Cold Spring Harbor Laboratory, New York  
    A. Zolli, Executive Director and Curator, PopTech, Camden, Maine

C. Heller, CEO, Heller Communication Design, Brooklyn, New York: Communi-cating for engagement.

M. Moon, Communication Designer, New York, New York: Art of the great presentation.

S. Marsh, Theatre Arts, Stony Brook University, New York: Improv for scientists—Robertson House.

M. Duenwald, Deputy Editor, Op-Ed Page, *The New York Times*, New York, New York: Demystifying the Op-Ed page.

L. Witter, Chief Strategy Officer, Fenton, New York: Media training.

H. Schneider, Dean, School of Journalism, Stony Brook University, New York: Communicating science in a changing media landscape.

Panel Discussion: The Journalists' Perspective

L. Cuthbert, Director, *Discovery News*, New York, New York

B. Nissen, Senior Producer, NBC News-NBC Learn, New York.

M. Moyer, Senior Technology Editor *Scientific American*, New York, New York and I. Oransky, Executive Editor, Reuters Health: *Science*, New York, New York: The journalist's perspective.

M. Nisbet, Associate Professor, School of Communication, American University, Washington, D.C. and R. Covey, Senior Vice President, National Geographic Digital Media, Washington, D.C.: Framing scientific issues to foster engagement.

G. MacKenzie, Founder and President, Gillian MacKenzie Agency, New York, New York; W. Murphy, Senior Editor, Random House, New York, New York; T. Neilsen, CEO, BrightSight Group, Princeton, New Jersey: Creating a personal brand.





# Plant Development and Phenomics

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September 19–22

FUNDED BY Cold Spring Harbor Laboratory/Pioneer–DuPont Joint Collaborative Research Program

ARRANGED BY D. Jackson, Cold Spring Harbor Laboratory, New York  
H. Sakai, Pioneer–DuPont International, Johnston, Texas

Every year, the Cold Spring Harbor Laboratory–DuPont Pioneer Collaborative meets to review current projects and to plan future projects. This year's update focused on the area of phenomics and its relation to plant development and included current research from outside the collaboration by speakers working in this field.

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

Introductory Remarks: D. Jackson, Cold Spring Harbor Laboratory, New York

S. Tingey, DuPont Experimental Station, Wilmington, Delaware

## SESSION 1: Informatics, Natural Variation, and Yield

Chairperson: Z. Lippman, Cold Spring Harbor Laboratory, New York

W. McCombie, Cold Spring Harbor Laboratory, New York: Novel sequencing methodologies and results.

B. Fendler, Cold Spring Harbor Laboratory, New York: Population genetics of microsatellites in humans.

D. Ware, Cold Spring Harbor Laboratory, New York: Profiling maize using next-generation sequencing approaches.

Z. Lippman, Cold Spring Harbor Laboratory, New York: Flowering, dosage, and yield.

R. Lafitte, Pioneer Hi-Bred International, Johnston, Iowa: Maize field phenotyping for transgene validation.

M. Williams, Dupont Experimental Station, Wilmington, Delaware: Identifying maternal haploid-inducing QTL1 and ENU-mutagenesis of maize.

## SESSION 2: Development, Epigenetics, and Networks

Chairperson: M. Aukerman, Dupont Experimental Station, Wilmington, Delaware

P. Bommert, Cold Spring Harbor Laboratory, New York: Cloning of compact Plant2 and update on other fasciated mutants.

M. Komatsu, DuPont Experimental Station, Wilmington, Delaware: Inflorescence traits and hybrid production.



- M. Aukerman, Dupont Experimental Station, Wilmington, Delaware: A putative silencing suppressor identified from an NUE screen.
- K. Creasey, Cold Spring Harbor Laboratory, New York: Developmental interaction of DDM1 and RNAi.
- J. Han, Cold Spring Harbor Laboratory, New York: Identification of high-copy mutator insertions in MTM lines by Illumina sequencing.

### SESSION 3: Phenomics and Shoot Development

**Chairperson: R. Williams**, DuPont Experimental Station, Wilmington, Delaware

- E. Spalding, University of Wisconsin, Madison: Root phenomics.
- T. Altmann, Leibniz Institute of Plant Genetics and Crop, Gatersleben, Germany: Analysis of *Arabidopsis* natural genetic variation and heterosis in biomass accumulation and metabolism.

### SESSION 4: Reproductive and Root Development

**Chairperson: D. Jackson**, Cold Spring Harbor Laboratory, New York

- J. Kyozuka, Tokyo University, Japan: Rice inflorescence development.
- U. Grossniklaus, Institute of Plant Biology University of Zurich, Switzerland: Genetic approaches toward the engineering of apomixis.
- D. Jackson, Cold Spring Harbor Laboratory, New York: Maize inflorescence development.

### SESSION 5: Epigenetics and General Discussion

**Chairperson: R. Martienssen**, Cold Spring Harbor Laboratory, New York

- A. Rafalski, Dupont Experimental Station, Wilmington, Delaware: Update on epigenotyping method development at Pioneer/Dupont.
- M. Regulski, Cold Spring Harbor Laboratory, New York: Epigenetic project.
- J. Lu, Cold Spring Harbor Laboratory, New York: Epigenetic project.

- A. Eveland, Cold Spring Harbor Laboratory, New York: Expression profiling of maize inflorescences.
- C. MacAlister, Cold Spring Harbor Laboratory, New York: Control of meristem size and identity at the transition to flowering in tomato: Role of terminating flower and fasciated flower.
- S. Kumari, Cold Spring Harbor Laboratory, New York: Genome-wide computational predications of core promoter elements in plant genomes.

- G. Li, Pioneer Hi-Bred International, Johnston, Iowa: HTP greenhouse phenotyping: Challenges and promises.
- Y. Eshed, Weizmann Institute of Science, Rehovot, Israel: Leaf development.
- M. Scanlon, Cornell University, Ithaca, New York: Maize shoot apical meristem genomics.

- G. Taramino, DuPont AgBiotechnology, Johnston, Iowa: Toward understanding the genetic network controlling maize root architecture.
- R. Martienssen, Cold Spring Harbor Laboratory, New York: Heterochromatin reprogramming and germ cell fate.
- S. Brady, University of California, Davis: Root networks.



S. Tingey



E. Spalding, S. Brady

# Fragile X Syndrome: Current Status, Future Prospects

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September 26–29

**FUNDED BY** University of Illinois through a grant from National Institute of Mental Health with additional support from the National Institute of Child Health and Human Development

**ARRANGED BY** K. Huber, University of Texas Southwestern Medical Center, Dallas  
P. Vanderklisch, Scripps Research Institute, La Jolla, California

The Banbury meetings on Fragile X syndrome have served as a major catalyst for the rapid advances the field has made over the last decade. These include elucidation of the molecular functions of FMRP; formation of the mGluR theory of Fragile X; expanded descriptions of behavioral phenotypes present in humans and animal models; identification of FMRP targets that have led to novel pathways for potential pharmacotherapy; and to several clinical trials. The present meeting was devoted to a critical review of where the field stands, to an examination of the current debates about mechanisms and treatments, and to determine the essential next steps.

**Welcoming Remarks:** J. Witkowski, Banbury Center, Cold Spring Harbor Laboratory, New York  
**Fragile X Portraits:** K. Clapp, FRAXA Research Foundation, Newburyport, Massachusetts

**SESSION 1: Clinical Trials and Outcome Measures**  
**Chairperson:** D. Nelson, Baylor College of Medicine, Houston, Texas

M. Tranfaglia, FRAXA Research Foundation, Newburyport, Massachusetts: Psychopharmacology of Fragile X: Past, present, and future.

R. Hagerman, University of California Davis Health System, Sacramento: Arbaclofen trial: Seaside study.

S. Webb, University of Washington, Seattle: Can EEG be used to assess response to medication?

E. Berry-Kravis, Rush University Medical Center, Chicago, Illinois: New outcome measures for clinical trials in FXS.

C. Erickson, Riley Hospital for Children, Indianapolis, Indiana: Commercially available glutamatergic agents in Fragile X syndrome: Pilot investigations.



## SESSION 2: Synapses, Circuits, and Rhythms

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

- D. Rojas, University of Colorado, Denver School of Medicine: Gamma-band responses as potential biomarkers in autism and FXS.
- W. Gan, New York University Medical Center, New York, New York: Abnormal experience-dependent dendritic spine plasticity in a mouse model of Fragile X.
- A. Contractor, Northwestern University, Chicago, Illinois: Synapse development in the sensory cortex of FMR1 knockout mice.
- M. Huntsman, Children's National Medical Center, Washington, D.C.: Inhibitory neurotransmission defects in Fragile X syndrome.
- L. Kaczmarek, Yale University School of Medicine, New Haven, Connecticut: FMRP, ion channels, and the regulation of neuronal timing.
- B. Alger, University of Maryland School of Medicine, Baltimore: Endocannabinoids and a mouse model of Fragile X syndrome.
- O. Manzoni, Neurocentre Magendie, Bordeaux, France: Disorganization of the endocannabinoid perisynaptic signaling machinery in FMR1<sup>-/-</sup> mice.
- R. Wong, SUNY-Downstate Health Science Center, Brooklyn, New York: Mechanism of mGluR-mediated plasticity.

## SESSION 3: Receptors to Ribosomes

**Chairperson: P. Vanderklish**, Scripps Research Institute, La Jolla, California

- K. Huber, University of Texas Southwestern Medical Center, Dallas: Mechanisms of mGluR5 dysfunction in Fmr1 KO mice.
- F. Tassone, Mind Institute, Davis, California: Altered mTOR-dependent signaling and differential mGluR expression patterns in Fragile X syndrome.
- S. Zukin, Albert Einstein College of Medicine, Bronx, New York: FMRP acts via PIKE to regulate mTOR signaling.
- G. Bassell, Emory University, Atlanta, Georgia: FMRP and miRNAs: Partners for translation at the synapse.

## SESSION 4: FMRP Isoforms and Their Manipulation in Brain

**Chairperson: I.J. Weiler**, University of Illinois, Urbana-Champaign

- D. Venkitaramani, University of Illinois, Urbana-Champaign: FMRP isoforms and restoration of function. Spatial, temporal, and splice variations in FMRP function.
- D. Nelson, Baylor College of Medicine, Houston, Texas: FMR1 and FXRs.

## SESSION 5: Targets and Model Systems

**Chairperson: G. Bassell**, Emory University, Atlanta, Georgia

- C. Westmark, Waisman Center, Madison, Wisconsin: Reversal of Fragile X phenotypes by manipulation of APP/A $\beta$  levels.
- R. Jope, University of Alabama, Birmingham: Therapeutic effects of GSK3 inhibitors in Fragile X mice.
- B. Oostra, Erasmus University, Rotterdam, The Netherlands: Rescue of behavioral phenotype and neuronal protrusion morphology in FMR1 KO mice.
- S. Haggarty, Massachusetts General Hospital, Boston: Using patient-specific iPS cells for modeling pathogenesis and treatment of Fragile X syndrome.
- P. Vanderklish, Scripps Research Institute, La Jolla, California: Strategies for new target discovery and evaluation. Identification and validation of new targets for the treatment of FXS.
- General Discussion: F. Gasparini**, Novartis Pharma AG, Basel, Switzerland



F. Tassone



D. Nelson



# Genome-Era Pathology, Precision Diagnostics, and Preemptive Care: A Stakeholder Summit

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October 13–15

FUNDED BY                Various institutions and individual participants

ARRANGED BY        M. Boguski, Beth Israel Deaconess Medical Center, Boston, Massachusetts  
                             J. Saffitz, Beth Israel Deaconess Medical Center, Boston, Massachusetts  
                             P. Tonellato, Beth Israel Deaconess Medical Center, Boston, Massachusetts

Historically, the discipline of pathology has had a central role to detect, classify, and interpret cellular and molecular markers of disease to guide physicians in the care and management of their patients. In recent years, many high-throughput technologies have been developed and used in research to determine the molecular and genetic mechanisms underlying diseases, but the pathology community has not responded systematically to the challenges and opportunities provided by these technological innovations. The objective of this discussion workshop was to define these opportunities, identify challenges and barriers to success, and formulate a call to action that will keep pathology at the forefront of modern medical care.

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

## SESSION 1: The Issue and Objective

**Welcome and Overview:** J. Saffitz, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts

### Brief Background Presentations

J. Schamberg, College of American Pathologists, Waukesha, Wisconsin: Pathology today: Challenges.

E. Green, National Human Genome Research Institute, Bethesda, Maryland: Genome-era pathology.

J. Saffitz, Beth Israel Deaconess Medical Center, Harvard Medical



School, Boston, Massachusetts: Genome-era pathology and preemptive care.

M. Boguski, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts

**Discussion:** Objectives of genome-era pathology

**Objective:** Define and refine primary objectives, open issues, and potential action items

## SESSION 2: Factors for Success

J. Crawford, North Shore LIJ Laboratories, Lake Success, New York

**Discussion:** Obstacles and challenges

**Objective:** Identify and prioritize primary challenges and identify potential solutions

P. Tonellato, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts and R. Haspel, Beth

Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts

**Discussion:** Overcoming the obstacles and challenges.

**Objective:** Review current efforts designed to resolve obstacles. Identify key stakeholders, approaches and methods to overcome barriers and funding options that may provide the resources and forums to act on solutions

## SESSION 3: A Call to Action

J. Crawford, North Shore LIJ Laboratories, Lake Success, New York, P. Tonellato, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, and M. Boguski, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts

**Discussion:** Summarize objectives, action items, and next steps

**Objective:** Summarize main points and final action items

J. Saffitz, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts

**Discussion:** The horizon view



S. Tomlins, F. Barr



W. Rosenkrans, R. Jeter, H. Halvorson

# Stem Cells, Genetics, and RNA-Binding Proteins: Recent Advances in ALS Research and Drug Discovery

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October 17–19

FUNDED BY           The ALS Association Greater New York Chapter

ARRANGED BY       L. Bruijn, The ALS Association, Washington, D.C.  
                          T. Maniatis, Columbia University Medical Center, New York, New York  
                          C. Svendsen, University of Wisconsin, Madison

During the past decade, significant progress has been made in understanding the mechanisms leading to ALS. The focus has shifted from a motor neuron centric view to a recognition that the neighboring cells and in particular the glia have an integral role in the disease process. The landscape for ALS is again changing, and this meeting brought together leaders in diverse fields of ALS genetics, RNA processing, stem cells, and model systems to discuss how to capitalize on the promising research advances in all these fields and make an impact on ALS discoveries. Progress in developing new in vitro and in vivo systems to better understand the disease and the development of new tools for drug discovery were key topics of discussion at the workshop. The workshop provided a unique opportunity for academic scientists, clinicians, and the industry to discuss how better to understand the role of the new genes in ALS and how this impacts drug discovery.



T. Maniatis

Introduction:       L. Bruijn, The ALS Association, Washington, D.C.

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



**SESSION 1: Genetics of ALS**

**Chairpersons:** C. Shaw, Guy's Hospital, London, United Kingdom and R. Brown, University of Massachusetts, North Worcester

**Overview of FUS/TDP43 Genetics and Pathology**

C. Shaw, Guy's Hospital, London, United Kingdom

R. Brown, University of Massachusetts, North Worcester

**Emerging Technologies in Genetics: Session Discussion**

J. Hardy, Reta Lila Weston Institute of Neurological Studies,  
University College London, United Kingdom

R. Myers, Hudson Alpha Institute for Biotechnology, Huntsville,  
Alabama

**SESSION 2: Disease Mechanisms and ALS**

**Chairperson:** A. Goldberg, Harvard Medical School, Boston, Massachusetts

**Disease Mechanism and Lessons Learned from SOD1**

D. Cleveland, University of California, San Diego, La Jolla

**Protein Misfolding and Cell Death: Apoptosis, Autophagy, and Necrosis**

A. Goldberg, Harvard Medical School, Boston, Massachusetts

D. Borchelt, University of Florida, Gainesville

**Glial-Neuronal Interactions and Inflammation**

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

B. Barres, Stanford University School of Medicine, California

**SESSION 3: Animal Models**

**Chairperson:** G. Cox, The Jackson Laboratory, Bar Harbor, Maine

R. Baloh, Washington University School of Medicine, St. Louis,  
Missouri

D. Cleveland, University of California, San Diego, La Jolla

P. Wong, Johns Hopkins University, Baltimore, Maryland

N. Shneider, Columbia University, New York, New York

**SESSION 4: TDP43/FUS and Disease Mechanism**

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

V. Lee, University of Pennsylvania School of Medicine,  
Philadelphia

M. Moore, HHMI/University of Massachusetts Medical School,  
Worcester

**SESSION 5: Stem Cells**

**Chairperson:** C. Svendsen, Cedar Sinai Medical Center, Los Angeles, California

**IPS Technology**

F. Soldner, Whitehead Institute, Massachusetts Institute of  
Technology, Cambridge

**IPS in ALS-Model Systems**

C. Svendsen, Cedar Sinai Medical Center, Los Angeles, California

K. Eggan, Harvard University, Cambridge, Massachusetts

**Assay Development Using Stem Cells**

H. Wichterle, Columbia University, New York, New York

D. Fischer, BioFocus DPI, Leiden, The Netherlands

S. Finkbeiner, University of California, San Francisco

**SESSION 6: Closing Session**

**Chairperson:** C. Svendsen, Cedar Sinai Medical Center, Los Angeles, California

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



J. Rothstein, D. Cleveland



# The Calculus of Medicine: Treatment of Pancreatic Cancer as a Prime Exemplar

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October 20–22

FUNDED BY                    Abraxis BioScience, Inc.

ARRANGED BY            J. Fleshman, Pancreatic Cancer Action Network, Manhattan Beach, California  
                                  B. Mishra, Courant Institute, New York University, New York, New York  
                                  P. Soon-Shiong, Abraxis BioScience, Inc., Los Angeles, California

This meeting emphasized the importance of the integration of computer science, statistics, and mathematics into biomedical research and clinical trials, focusing on a better understanding of cancer, with pancreatic cancer as the prime exemplar. Key leaders in oncology research and clinical application discussed how to shape this exciting field (and community) with a particular focus on genomics, proteomics, imaging, translational bioinformatics, systems biology, disease modeling, single-cell analysis and nano-medicine.

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

Introductory Remarks: J.-P. Bizarri, Celgene, Summit, New Jersey

## SESSION 1: The Biology of Pancreatic Cancer

Chairperson: D. Tuveson, CRUK Cambridge Research Institute, United Kingdom

R. Hruban, Johns Hopkins Medical Institutions, Baltimore, Maryland: Genetics of pancreatic cancer.

D. Simeone, University of Michigan Health Systems, Ann Arbor: Pancreatic stem cells.

D. Bar-Sagi, New York University, New York, New York: Inter- and intra-cellular pathways in PDA.

D. Hedley, Ontario Cancer Institute, Toronto, Canada: Effects of the tumor microenvironment on invasion and metastasis.



D. Tuveson, CRUK Cambridge Research Institute, United Kingdom: Stromal barriers in pancreatic cancer.

M. Lisanti, Kimmel Cancer Center, Philadelphia, Pennsylvania: Warburg in reverse: The autophagic tumor stroma model of cancer.

M. Lotze, University of Pittsburgh, Pennsylvania: Autophagy as a target in pancreatic cancer.

## **SESSION 2: Clinical Developments in Pancreatic Cancer**

**Chairperson: M. Tempero**, University of California, San Francisco

M. Tempero, University of California, San Francisco: New paradigms for drug development.

J. Berlin, Vanderbilt-Ingram Cancer Center, Nashville, Tennessee: New agents for treatment of pancreatic cancer.

M. Hidalgo, Centro Nacional de Investigaciones Oncologicas, Madrid, Spain: Targeting the stroma in pancreatic cancer.

P. Philip, Karmanos Cancer Institute, Detroit, Michigan: Targeting IGF-IR in pancreatic cancer.

J. Clark, Massachusetts General Hospital, Boston: Modulating KRAS as a target in pancreatic cancer.

W. Isacoff, University of California, San Francisco: Novel chemotherapy schedules for pancreatic cancer.

## **SESSION 3: BioInformatics and BioMarkers in Pancreatic Cancer**

**Chairperson: B. Mishra**, Courant Institute, New York University, New York, New York

C. Cantor, Sequenom Inc., San Diego, California: Cancer-specific nucleic acid sequences.

J. Reed, University of California, Los Angeles: Nano measurement approaches for characterizing single cells in populations.

B. Mishra, Courant Institute, New York University, New York, New York: Translational cancer bioinformatics.



J. Watson, L. Lisanti



D. Bar-Sagi, D. Simeone

# Energy Metabolism, the Cell Cycle, and Cancer

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October 31–November 3

FUNDED BY            Oliver Grace Cancer Fund

ARRANGED BY        D. Beach, Barts and London School of Medicine & Dentistry, United Kingdom  
                             L. Cantley, Beth Israel Deaconess Medical Center, Boston, Massachusetts  
                             B. Futcher, Stony Brook University, New York

In 1924, Otto Warburg drew attention to the fact that cancer cells generate energy largely through glycolysis and he believed that this was the fundamental characteristic of cancer cells. In recent years, there has been a renewal of interest in the Warburg effect, and this meeting focused on the general idea that proliferating cells may require more energy than quiescent cells and that energy production must therefore be coordinated with commitment to cell cycle entry. Specific topics included the Warburg effect; TOR and AKT signaling; metabolites controlling gene expression, energy metabolism, and the cell cycle; and effects of oxygen and reactive oxygen species. Although the meeting concentrated on mammalian systems, recent results from model systems such as yeast showing linkages between energy metabolism and cell cycle were also discussed.

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

**Introductory Remarks:** C. Van Dang, Johns Hopkins Medical School, Baltimore, Maryland

## SESSION 1: Glycolysis and Energy

**Chairperson:** J. Blenis, Harvard Medical School, Boston, Massachusetts

J. Chesney, University of Louisville, Kentucky: Fructose-2, 6-bisphosphate couples glycolysis with proliferation.

C. Van Dang, Johns Hopkins Medical School, Baltimore, Maryland: Oncogenic alterations of glucose and glutamine metabolism.

M. Vander Heiden, Massachusetts Institute of Technology, Cambridge: PKM2 and understanding the energetics of cancer cell metabolism.

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

The LKB1/AMPK pathway: Tumor suppression and central regulators of metabolism.

M. Pollak, SMBD Jewish General Hospital, Montreal, Quebec, Canada: Host energy intake, cellular energy supply, and tumor growth: Roles of insulin and AMPK.

K. Struhl, Harvard Medical School, Boston, Massachusetts: Metformin selectively kills cancer stem cells and acts together with chemotherapy to prolong remission.



## SESSION 2: Metabolic Regulation

**Chairperson:** J. Chesney, University of Louisville, Kentucky

- Y. Xiong, University of North Carolina, Chapel Hill: Metabolic regulation in normal and tumor cells.  
 M. Lisanti, Kimmel Cancer Center, Philadelphia, Pennsylvania: Warburg in reverse: The autophagic tumor stroma model of cancer.

J. Brugge, Harvard Medical School, Boston, Massachusetts: Regulation of metabolism by extracellular matrix on oncogenes.

## SESSION 3: PI3 Kinase, Isocitrate Dehydrogenase, TOR

**Chairperson:** L. Cantley, Beth Israel Deaconess Medical Center, Boston, Massachusetts

- L. Cantley, Beth Israel Deaconess Medical Center, Boston, Massachusetts: PI3 kinase and cancer metabolism.  
 D. Schenkein, Agios Pharmaceuticals, Cambridge, Massachusetts: Mutations in isocitrate dehydrogenase: Role in disease pathogenesis and potential as a therapeutic target.  
 T. Mak, Campbell Family Institute for Breast Cancer Research at PMH, UHN, Toronto, Ontario, Canada: Knock-in mouse model for IDH1 mutations.

- J. Blenis, Harvard Medical School, Boston, Massachusetts: Amino acids, mTOR signaling, and metabolism.  
 B. Manning, Harvard University, Boston, Massachusetts: mTOR activation drives the metabolic reprogramming of tumor cells.  
 M. Tyers, University of Edinburgh, United Kingdom: Metabolic and growth control by TOR effectors in yeast.

## SESSION 4: Connections between Metabolism and Cell Cycle in Yeast

**Chairperson:** M. Tyers, University of Edinburgh, United Kingdom

- B. Futcher, Stony Brook University, New York: Introductory remarks.  
 B. Tu, University of Texas Southwestern Medical Center, Dallas: Metabolic signals that drive cell growth and proliferation.  
 A. Caudy, Princeton University, New Jersey: The sedoheptulose biphosphatase SHB17 shunts carbon from glycolysis to the pentose phosphate pathway for riboneogenesis in yeast.

- J. Broach, Princeton University, New Jersey: Direct control of metabolism by nutrient signaling pathways in yeast.  
 B. Futcher, Stony Brook University, New York: cAMP, liquidation of storage carbohydrates, and commitment to the cell cycle.  
 S. Kohlwein, Karl-Franzens-Universität Graz, Austria: Lipid requirements during the cell cycle.

## SESSION 5: Cancer Metabolism and p53

**Chairperson:** L. Cantley, Beth Israel Deaconess Medical Center, Boston, Massachusetts

- E. White, Cancer Institute of New Jersey, New Brunswick: Role of autophagy in cancer metabolism.  
 K. Vousden, Beatson Institute for Cancer Research, Bearsden, Glasgow: The regulation of metabolism by p53.

- A. Levine, Institute for Advanced Study, Princeton, New Jersey: Role of p53 in regulating metabolic pathways.  
 L. Cantley, Beth Israel Deaconess Medical Center, Boston, Massachusetts: Concluding remarks and general discussion.



J. Brugge



D. Schenkein



A. Caudy



# Easeful Death: 21st Century Perspectives on Assisted Suicide

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November 3–5

FUNDED BY            The Ellison Medical Foundation

ORGANIZED BY    M. Battin, University of Utah, Salt Lake City  
                         E. MacDonald, Guy's and St. Thomas Hospital, London, United Kingdom  
                         T. Murray, The Hastings Center, Garrison, New York, New York  
                         M. Raff, University College London, United Kingdom  
                         J. Witkowski, Banbury Center, Cold Spring Harbor Laboratory, New York

Because of advances in medical care, the proportion of the elderly in the population is increasing. And as a consequence, the number of individuals suffering from Alzheimer's, Parkinson's, and motor neuron diseases, as well as other age-related degenerative disorders, is increasing. Individuals suffering from these disorders place an extraordinary burden on their caregivers, who are often also elderly and who may be unable to cope. End-of-life issues involve profound legal, moral, religious, and biomedical questions and evoke such intense passions that calm discourse is hard to achieve. The Banbury Center provided a venue for calm discussions of topics, which included what are the data on assisted suicide and how (and why) do interpretations of the data differ? What is the evidence for abuse, what is its incidence and how might it be prevented? How can end-of-life decisions be made in cases of psychiatric illness (and perhaps dementia)? Participants included scientists, physicians, philosophers, lawyers, and religious leaders and included experts on euthanasia and assisted suicide in Europe.

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

Introductory Remarks:    M. Raff, University College London, United Kingdom



## SESSION 1

**Chairperson:** T. Murray, The Hastings Center, Garrison, New York

M. Battin, University of Utah, Salt Lake City: Discussion.

B. Gert, Dartmouth College, Hanover, New Hampshire: Refusal of hydration and nutrition as an alternative to physician-assisted suicide.

D. Orentlicher, University of Iowa, Iowa City: Drawing lines at the end of death: Where can we draw meaningful lines among treatment withdrawal, assisted suicide, and euthanasia?

## SESSION 2

**Chairperson:** E. MacDonald, Guy's and St. Thomas Hospital, London, United Kingdom

B. Onwuteaka-Philipsen, VU Medical Center, Amsterdam, The Netherlands: The influence of regulation on the practice of assisted suicide in The Netherlands.

L. Deliens, Vrije Universiteit, Brussels, Belgium: Belgian data on euthanasia.

L. Cohen, Baystate Medical Center, Northampton, Massachusetts: Accusations and investigations of euthanasia and PAS directed at American palliative medicine physicians.

**Matters arising from Day 1**

## SESSION 3

**Chairperson:** R. Payne, Duke Divinity School, Durham, North Carolina

C. Baron, Boston College, Newton, Massachusetts: Law at the end of life: Have we come of age?

J. Lynn, Colorado Foundation for Medical Care, Chevy Chase, Maryland: Political realities and strategies: Improving care in the "death panel" era.

**General Discussion:** What is the 21st perspective on assisted suicide?



J. Prey, M. Raff



L. Deliens, T. Murray



Z. Schostak, B. Gert

# Microbial Forensics in the Era of Genomics

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November 7–10

FUNDED BY           The U.S. Department of Homeland Security and individual participants

ARRANGED BY       B. Budowle, University of North Texas Health Science Center, Fort Worth  
                          T. Pals, U.S. Department of Homeland Security, Washington, D.C.  
                          S. Schutzer, University of Medicine and Dentistry–New Jersey Medical School, Newark

This workshop brought experts in metagenomics together with experts from the field of microbial forensics and bioterrorism to consider the implications of whole-genome sequencing for investigations of bioterrorism. It is likely that whole-genome sequencing will become the method of choice to characterize a microbe and compare it with a reference sample. However, there are issues when considering strategic planning and implementation of genome-wide analyses for forensic attribution purposes. These include the development of reference databases for making inferences about the significance of an observation; the need to establish criteria to guide decision makers and scientists on performance and expectations; how to deal with degraded and trace evidence; how to improve analytical and sampling strategies for maximum extraction of information from large data sets; and cost.

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

## SESSION 1: Overview

**Chairperson:** S. Schutzer, University of Medicine and Dentistry–New Jersey Medical Center, Newark

B. Budowle, University of North Texas Health Science Center,  
Fort Worth: Microbial forensics in the era of genomics: Setting  
the stage.

T. Pals, U.S. Department of Homeland Security, Washington,  
D.C.: Bioforensics basic research R&D program.

R. Murch, Virginia Tech–National Capital Region, Alexandria:  
Overview of needs.



**Discussion:**

**Leaders:**

N. Bergman, National Biodefense Analysis and Countermeasures Center, Frederick, Maryland and A. Phillippy, Battelle National

Biodefense Institute, Frederick, Maryland: Current analytical and bioinformatic tools available to meet the national mandate for characterization of microbial forensic evidence.

**SESSION 2: Lessons from Case Studies**

**Chairperson:** B. Budowle, University of North Texas Health Science Center, Fort Worth

R. Bull, Federal Bureau of Investigation, Frederick, Maryland:

Lessons learned from anthrax attack and other cases.

D. Rock and W. Laegreid, College of Veterinary Medicine, Urbana,

Illinois: Lessons not learned from animal agriculture cases.

T. Cebula, Johns Hopkins University, Baltimore, Maryland:

Lessons learned from human food outbreaks.

**SESSION 3: Technology: What Do We Currently Have and What Do We Need? If Money Is No Object;**

Philosophy/Fantasy

**Chairperson:** P. Pesenti, U.S. Department of Homeland Security, Washington, D.C.

P. Keim, Northern Arizona University, Flagstaff: Whole-genome sequencing, targeted genotyping, and the value of databases for investigation of plague infections.

W. Nierman, J. Craig Venter Institute, Rockville, Maryland:

Forensic sequencing project accuracy with current sequencing production platforms and assembly and analysis tools.

J. Ravel, Institute of Genome Sciences, University of Maryland, Baltimore: Real-time or targeted marker typing capabilities.

C. Fraser-Liggett, University of Maryland School of Medicine, Baltimore: Current technologies and wish list.

W. McCombie, Cold Spring Harbor Laboratory, New York: Overview of bioinformatic capabilities.

**SESSION 4: Quality of Sample of Necessary Technology**

**Chairperson:** J. Burans, U.S. Department of Homeland Security, Frederick, Maryland

M. Eshoo, Ibis Biosciences, Inc. Carlsbad, California: Extraction capabilities, DNA repair, and whole-genome amplification and

analysis of trace unculturable specimens.



B. Budowle, A. van Daal, J. Smith, S. Schutzer, T. Cebula



# SESSION 5: Other Technologies Including Proteomics

**Chairperson:** S. Morse, Centers for Disease Control & Prevention, Atlanta, Georgia

S. Velsko, Lawrence Livermore National Laboratory, California:  
Nongenetic technologies.  
T. Angel, Pacific Northwest National Laboratory, Richland,

Washington: Proteomic complements to genomics.  
R. Bull, Federal Bureau of Investigation, Frederick, Maryland:  
Potential host forensic signatures.

# SESSION 6: Metagenomics

**Chairperson:** C. Fraser-Liggett, University of Maryland School of Medicine, Baltimore

G. Weinstock, Washington University School of Medicine, St.  
Louis, Missouri: Metagenomics for surveillance.  
J. Ravel, Institute for Genomic Research, University of Maryland,  
Baltimore: Human microbiome.  
Y. Fofanov, University of Houston, Texas: Software and  
analytical tools.

A. van Daal, Bond University, Gold Coast, Australia: Example of  
specific platform (Illumina HiSeq) capabilities to meet needs of  
microbial forensics.

# SESSION 7: Bioinformatics

**Chairperson:** P. Keim, Northern Arizona University, Flagstaff

S. Velsko, Lawrence Livermore National Laboratory, California:  
What questions need to be answered?  
J. Tiedje, Michigan State University, East Lansing: Population  
genetics issues.  
R. Chakraborty, University of North Texas Health Science, Fort  
Worth: Statistical interpretation issues: Comparison to forensic  
human DNA.

T. Leighton, Children's Hospital, Oakland Research Institute,  
California: Next-generation DNA sequencing analysis of clonal  
variants, manipulated populations, and production process  
trace-back.  
S. Velsko, Lawrence Livermore National Laboratory, California:  
Genetic inference on disease transmission networks.

# SESSION 8: Data Sharing

**Chairperson:** D. Rock, College of Veterinary Medicine, Urbana, Illinois

T. Slezak, Lawrence Livermore National Laboratory, California:  
Forensic uses of microarrays or databases for sharing forensic  
data.  
B. Budowle, University of North Texas Health Science Center,  
Fort Worth: Archives and database needs.

J. Smith, Penn State University, Pennsylvania; BioForensic  
Consulting, LLC, Edgewood, Maryland: Data exchange  
requirements and policies for sharing.  
C. Cooke Jr., WINPAC, Washington, D.C.: Quality assurance for  
data generation.

# SESSION 9: Summary

**Chairperson:** S. Schutzer, University of Medicine and Dentistry–New Jersey Medical School, Newark

B. Budowle, University of North Texas Health Science Center,  
Fort Worth and Traci Pals, U.S. Department of Homeland  
Security, Washington, D.C.: Prioritization of needs, recap, wrap

up, strategies, and what we would like conveyed to the  
community, stakeholders, policy makers, and summary for  
manuscript.

# Signaling through Ubiquitin

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November 14–17

FUNDED BY            The Cold Spring Harbor Laboratory Corporate Sponsor Program

ARRANGED BY        R. Deshaies, California Institute of Technology, Pasadena  
                             V. Dixit, Genentech, South San Francisco, California  
                             W. Tansey, Vanderbilt University Medical Center, Nashville, Tennessee

The object of this meeting was to analyze and discuss how protein ubiquitylation exerts its myriad of biological effects within the cell. Although ubiquitin has traditionally been studied within the context of protein turnover, it is now clear that ubiquitylation refers to a complex set of posttranslational modifications that are interpreted by the cellular machinery to impact a broad range of biological processes, just one of which is proteolysis. Participants in the meeting discussed the spectrum of ubiquitin and related modifications, how they are recognized, and what they do. Discussions drew on experts in biochemistry, cell biology, computational biology, structural biology, genetics, and pathophysiology to identify common emerging themes in how ubiquitin and related proteins work.

Introductory and Welcoming Remarks:    J. Witkowski, Banbury Center, Cold Spring Harbor Laboratory, New York  
Introductory Remarks:                        W. Tansey, Vanderbilt University Medical Center, Nashville, Tennessee

**SESSION 1: Signaling via Ubiquitin Chain Diversity and Recognition**  
Chairperson: T. Hunter, The Salk Institute, La Jolla, California

R. Cohen, Colorado State University, Fort Collins: Recognition of polyubiquitin chains.  
K. Hofmann, Miltenyi Biotec GmbH, Gladbach, Germany: UBL receptors: At the crossroads of UPS and autophagy.  
S. Polo, Institute of Molecular Oncology Foundation, Milan, Italy: Specificity in chain formation and recognition.  
Z. Chen, University of Texas Southwestern Medical Center,

Dallas: Ubiquitin signaling in the RIG-I antiviral pathway.  
I. Dikic, Johann Wolfgang Goethe University Medical School, Frankfurt, Germany: Ubiquitin signaling networks.  
K. Iwai, Osaka University, Japan: Linear polyubiquitination: A new regulator of NF- $\kappa$ B signaling.  
J. Peng, Emory University School of Medicine, Atlanta, Georgia: Exploring ubiquitin pathways by quantitative proteomics.



**SESSION 2: Signaling via Ub-Like Proteins**

**Chairperson: M. Hochstrasser**, Yale University, New Haven, Connecticut

- R. Hay, Sir James Black Centre, University of Dundee, United Kingdom: SUMO targeted ubiquitin ligases.
- J. Huijbregtse, University of Texas, Austin: The mechanism and function of ISG15 conjugation.
- T. Hunter, The Salk Institute, La Jolla, California: Ubiquitin-SUMO cross-talk.
- C. Lima, Memorial Sloan-Kettering Cancer Institute, New York, New York: Structure and mechanism in the SUMO conjugation pathway.
- Y. Ohsumi, Frontier Research Center, Tokyo Institute of Technology, Yokohama, Japan: Two ubiquitin-like conjugation reactions essential for autophagy.
- A. Huang, Sanofi-Aventis, Cambridge, Massachusetts: Regulation of axin stability through poly-ADP ribosylation: Linking Wnt pathway signaling activity, ubiquitination, and poly-ADP-ribosylation.

**SESSION 3: Signaling to the Proteasome**

**Chairperson: J. Huijbregtse**, University of Texas, Austin

- D. Finley, Harvard Medical School, Boston, Massachusetts: Editing of ubiquitin at the proteasome.
- M. Glickman, Technion-Israel Institute of Technology, Haifa, Israel: Coordination of ubiquitin-processing factors at the proteasome.
- M. Hochstrasser, Yale University, New Haven, Connecticut: Proteases of the ubiquitin system.
- R. Kopito, Stanford University, California: Why do ubiquitin chains accumulate in neurodegenerative disease?
- S. Murata, The University of Tokyo, Japan: Proteasome diversity.
- R. Deshaies, California Institute of Technology, Pasadena: Ned8 links active Cullin-RING ligases to p97 substrate processing machinery.

**SESSION 4: Ubiquitin-Proteasome Signaling in the Nucleus**

**Chairperson: R. Hay**, Sir James Centre, University of Dundee, United Kingdom

- G. Rosenfeld, University of California, San Diego, La Jolla: Ubiquitylation, SUMOylation, methylation, and strategies in regulated transcriptional programs.
- W. Tansey, Vanderbilt University Medical Center, Nashville, Tennessee: Ubiquitin and transcription.
- H. Ulrich, Cancer Research UK, London Research Institute, Herts, United Kingdom: Ubiquitin and replication stress.

**SESSION 5: Ubiquitin Signaling in Disease States**

**Chairperson: R. Kopito**, Stanford University, California

- A. D'Andrea, Dana-Farber Cancer Institute, Boston, Massachusetts: Regulation of the Fanconi anemia pathway to deubiquitination.
- R. Youle, National Institute of Health, Bethesda, Maryland: Mechanisms of Parkin-mediated mitophagy.

**SESSION 6: Ub-Ligases, Isopeptidases, and Their Substrates**

**Chairperson: C. Lima**, Memorial Sloan-Kettering Cancer Institute, New York, New York

- V. Dixit, Genentech, South San Francisco, California: Ubiquitin modification in cancer.
- W. Harper, Harvard Medical School, Boston, Massachusetts: Signaling through the ubiquitin-proteasome pathway.
- M. Pagano, New York University School of Medicine, New York, New York: SCF ubiquitin ligases and cell proliferation.
- P. Kaiser, University of California, Irvine: Interpretation of ubiquitin signal.
- P. Matthias, ETH Zurich, Institute of Biochemistry, Switzerland: Regulation and substrates of Cullin-based E-3 ligases.
- M. Rape, University of California, Berkeley: Role of lysine 11-linked ubiquitin chains in cell cycle control.
- B. Schulman, St. Jude Children's Research Hospital, Memphis, Tennessee: Structural studies of Cullin-RING ligases.

# DNA, Genetics, and the History of Mankind

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November 28–30

FUNDED BY            The Lehrman Institute

ARRANGED BY        J. Witkowski, Banbury Center, Cold Spring Harbor Laboratory, New York

The impact of molecular genetic studies has spread beyond the immediate discipline of biology, and as the study of genetic variation is essentially an historical study, DNA analysis has been applied to historical problems in related disciplines. For example, conclusions on the movements of early human populations based on linguistic and archeological data have been reinforced or modified by DNA analysis. Domestication of animals and plants marked one of the great transitions in human history, and genetic analysis is revealing how and where domestication took place. Genetic analysis may provide reliable information on personal relationships and identification that has been the subject of speculation, for example, Thomas Jefferson's family and identifying the bodies of the Tsar's family. Participants in this workshop discussed how genetic and DNA analysis can further our understanding of the history of human beings, and how to promote such studies.

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

## SESSION 1

Chairperson: M. Thomas, University College London, United Kingdom

K. Dobney, University of Aberdeen, United Kingdom and J.-D.  
Vigne, Muséum National d'Histoire Naturelle, Paris, France:

Mammals to microbes: Role of genetics in exploring past bio-  
cultural dynamics using the fossil vertebrae record.





- E. Willerslev, Natural History Museum of Denmark, Copenhagen: Early peopling of the New World and extinction of the megafauna.
- M. Richards, University of Leeds, United Kingdom: Archaeogenetics and modern human dispersals.
- C. Bustamante, Stanford School of Medicine, California: Sequencing admixed genomes and what the thousand genomes data are telling us.

- A. Chakravarti, Johns Hopkins University School of Medicine, Baltimore, Maryland: Admixture: What it means for studying human populations.
- B. Shapiro, Pennsylvania State University, University Park: Appropriately incorporating spatial and temporal information into genealogical analysis.
- W. McCombie, Cold Spring Harbor Laboratory, New York: Human genetics in the era of “next-generation” sequencing.

## SESSION 2

**Chairperson:** J. Buikstra, Center for Bioarchaeological Research, Arizona State University, Tempe

- S. Pääbo, Max-Planck Institute for Evolutionary Anthropology, Leipzig, Germany: The contributions of DNA studies: What we would not, and could not, have gained from other sources.
- D. Reich, Harvard Medical School, Boston, Massachusetts: Evidence for gene flow from neanderthals into modern humans.
- J. Hawks, University of Wisconsin, Madison: Natural selection, population growth, and human migrations in the early holocene.

- M. Crawford, University of Kansas, Lawrence: The sequelae of Russian contact in the Aleutian archipelago: Molecular perspectives.
- M. Zeder, National Museum of Natural History, Washington, D.C.: Documenting domestication: The intersection of archaeology and genetics.
- A. Stone, Arizona State University, Tempe: The origins and spread of human tuberculosis.

## SESSION 3

**Chairperson:** L. Madrigal, University of South Florida, Tampa

- N. Wade, *The New York Times*, New York, New York: The evolution of human races and economic systems.
- D. O'Rourke, University of Utah, Salt Lake City: Consultation

and consent: Cultural concerns in human population genetic research.

## SESSION 4: Future Developments

- J.-D. Vigne, Muséum National d'Histoire Naturelle, Paris, France: The Archaeozoology and Genetics (A&G) Working Group of International Council for Archaeozoology (ICAZ).
- D. O'Rourke, University of Utah, Salt Lake City: The American Association of Physical Anthropologists.
- J. Witkowski, Banbury Center, Cold Spring Harbor Laboratory, New York

### Discussion Points

- What might be done to foster cross-disciplinary interactions in these fields?
- What topics should be covered in a Banbury Center meeting in 2011?
- Any other points for discussion?



D. Micklos, S. Pääbo, D. Reich, B. Shapiro

**BANBURY CENTER GRANTS**

<i>Grantor</i>	<i>Program</i>	<i>Duration of Grant</i>	<i>2010 Funding</i>
<b>FEDERAL SUPPORT</b>			
NIH–National Institute of Mental Health	The 2nd Annual NIMH–Sponsored Brain Camp	2010	\$ 44,465
U.S. Department of Homeland Security	Microbial Forensics in the Era of Genomics	2010	23,433
<b>NONFEDERAL SUPPORT</b>			
Abraxis Bioscience, Inc.	The Calculus of Medicine: Treatment of Pancreatic Cancer as a Prime Exemplar	2010	41,955
Alfred P. Sloan Foundation	How Can We Maintain the Stability of Biomedical Research and Development at the End of the ARRA?	2010	9,891
ALS Association	Stem Cells, Genetics, and RNA-Binding Proteins: Recent Advances in ALS Research and Drug Discovery	2010	32,231
Champalimaud Foundation and the Champalimaud Metastasis Programme	Tumor Microenvironment and Metastasis	2010	35,407
Cold Spring Harbor Laboratory Corporate Sponsor Program	Epigenetic Reprogramming and Trans-Generational Inheritance	2010	52,673
Cold Spring Harbor Laboratory Corporate Sponsor Program	Signaling through Ubiquitin	2010	45,994
Cold Spring Harbor–Pioneer Collaborative Research Program	Plant Development and Phenomics	2010	54,394
Columbia University	p53 Retreat	2010	10,870
Ellison Medical Foundation	Easeful Death: 21st Century Perspectives on Assisted Suicide	2010	25,374
Howard Hughes Medical Institute	How Can We Maintain the Stability of Biomedical Research and Development at the End of the ARRA?	2010	10,000
The Lehrman Institute	DNA, Genetics, and the History of Mankind	2010	29,755
Marie Robertson Research Fund	The Lateral Habenula: Its Role in Behavior Molecules to Mood	2010	40,000
Oliver Grace Fund	Linguistic Phenotypes: Toward a Biological Understanding of Language	2010	31,472
Oliver Grace Cancer Fund	Mutagenesis: What It Means and How It Has changed	2010	39,357
Oliver Grace Cancer Fund	Energy Metabolism, the Cell Cycle, and Cancer	2010	40,912
PopTech Accelerator	PopTech Fellows Retreat	2010	42,000
Simons Foundation	Linguistic Phenotypes: Toward a Biological Understanding of Language	2010	10,000
United Biomedical, Inc.	Genetic Variation at a Single Locus for Prediction and Prevention of Late-Onset Alzheimer's Disease	2010	14,275
Université de Québec	Linguistic Phenotypes: Toward a Biological Understanding of Language	2010	3,000
University of Illinois	Fragile X Syndrome: Current Status, Future Prospects	2010	48,306
Various institutions and individuals	Genome Era Pathology, Precision Diagnostics, and Preemptive Care	2010	22,260