Banbury Center cold spring harbor laboratory 2001



BANBURY CENTER DIRECTOR'S REPORT

The Banbury Center continues to be used almost year-round. There were 26 meetings in the Banbury meetings program, and Laboratory staff came to the Center for seven internal meetings. The graduate students of The Watson School of Biological Sciences held in March a week-long course on evolution, and local community groups used our facilities on five occasions. Of the more than 650 participants in the meetings in 2001, 104 (14%) came from abroad. American participants came from 40 states, with 3 states—New York, California, and Maryland—providing one third of the visitors. The program of meetings was, as usual, catholic in its range of topics.

Science Policy

Napster is a good example of how the Internet is making, and provoking, extraordinary changes in the dissemination of anything that can be digitized. The world of scientific publishing is not immune from these changes and *Electronic Access to Scientific Literature* (John Inglis and Jan Witkowski, April 16–18) was held to examine ideas and initiatives intended to lower the barriers to electronic access to the scientific literature. Stimulated by the PubMed Central Initiative, the participants examined this and its implications for commercial publishers.

Great hope is being held for the applications of genomics to health care. This depends on having not only the sequence of the human genome, but also appropriate technologies for using that information and, just as importantly but often neglected, the appropriate health care and regulatory policies. The purpose of *Integrating Genomics Technologies in Health Care: Practice and Policy Challenges* (Finley Austin and Thame Kreiner, February 25–28) was to assess where the technology is heading; to educate participants in what is happening in fields other than their own; and to consider broader issues such as social impact, safety, and oversight.

Another health care area where practical applications are heavily dependent on policy is in vaccine development. *Making Vaccines for the Developing World: Access to and Deployment of New Technologies* (Melinda Moree and Philip K. Russell, October 9–11) examined the ways in which early access to enabling technologies is important for efficient and cost-effective vaccine development. There may be difficulty in gaining such access except in cases where the price of the vaccine can be set to pay for royalties on enabling technologies. There was discussion of what can be done to promote partnerships between public sector vaccine developers and the technology companies.

Genomics

The availability of complete genome sequences has spurred a tremendous increase in sequence analysis, but this is being done largely on an ad hoc basis, with Web Sites using different sets of nomenclature rules, query systems, and user interfaces. The information becomes fragmented, and it is difficult for biologists to know what is available. The *Genomic Annotation Workshop: DNA Replication* (Lincoln Stein and Ewan Birney, March 17–22) was the first in a series of workshops that will take a well-circumscribed topic—in this case DNA replication—and bring biologists expert in the topic together with informaticists. Together, they will create curated annotations of the genome that summarize the current state of knowledge in the field. The workshop was very successful and the results were presented at the *DNA Replication* meeting.

Cancer

Three meetings on cancer were held at Banbury in 2001, all dealing with important issues in cancer treatment. Two—Interferons: Biological Mechanisms and Disease Treatments I and II—dealt with the



Meier House provides accommodations for meeting participants at Banbury Center.

clinical uses of interferon. Organized by Josh Fidler, and by Ernest Borden and Judah Folkman, respectively, the meetings were particularly interesting in that they were not restricted to interferon and cancer, but reviewed the actions of interferon in virus infections as well as in multiple sclerosis. The meetings also discussed the clinical trials of interferon and whether extending the findings to multi-institutional Phase II trials will yield insights into the biology, pathology, and mechanisms of antitumor actions of interferons.

New Concepts for Clinical Cancer Trials (Douglas Hanahan, Jan Witkowski, Judah Folkman, Robert Kerbel, and Jim Pluda, November 4–7) discussed new findings indicating that the manner in which cancer treatments are given is important. It seems that different dosing schedules combined with lower doses could increase the efficacy and reduce the toxicity and side effects of traditional cytotoxic drugs, and perhaps also of radiotherapy and some investigational drugs. However, whereas a maximum tolerated dose is relatively easy to establish, it is not as clear how to determine optimal dosing at the lowest possible levels while maintaining maximal efficacy in these kinds of schedules. The possible benefits for patients are so great that these problems must be overcome.

The J.P. Morgan H&Q Executives Conference

David Deming and J.P. Morgan H&Q continue to support what is one of the highlights of the Banbury Center year. This year's meeting—*Controlling Cancer*—tackled the controversial idea that an all-out war on a patient's cancer by chemotherapy, radiation, and surgery—all of which cause considerable suffering to the patient—may not be the best strategy. Instead, it may be possible to contain cancer, treating it as a chronic disease. We had a marvelous set of speakers including Doug Hanahan, Scott Lowe, Bob Kerbel, Kari Alitalo, Raghu Kalluri, Brian Sawyers, and Joseph Schlessinger.

Neuroscience

The two Banbury Center meetings on neuroscience dealt with contrasting aspects of brain function. One—*Cortical Maps* (Dmitri Chklovskii and Alexei Koulakov, October 13–16)—was primarily experimental. The goal of the meeting was to stimulate discussion between neuroscientists working on different aspects of cortical maps: theoretical and experimental, physiological and anatomical, and developmental and functional.

In contrast, *Can a Machine Be Conscious*? (David Chalmers, Rod Goodman, Owen Holland, Christof Koch, and Jerome Swartz, May 13–16) dealt with a topic with strong psychological and philosophical underpinnings. A wealth of new experimental information about the brain has been gathered by neuroscientists, and the organizers felt that the time was ripe for a meeting to discuss how these data inform classic thinking on consciousness. The topic was focused by considering the design and construction of a conscious machine. Could a machine ever be said to be conscious? Or is consciousness something only biologically evolved animals and humans can ever possess?

Biology

Meetings on basic research in biology are the foundation of the Banbury Center program, and there were some especially interesting meetings in this category in 2001.

Discovered 10 years ago, various families of seven-transmembrane receptor genes have been identified that encode chemosensory receptors, for example, nematode and fruit fly odorant receptors, vomeronasal receptors, and taste receptors. With recent advances in genome sequencing projects, genome-wide studies of these families have become feasible. However, no meetings have been dedicated to the molecular biology of chemosensory receptor genes, which form the largest known gene families in animal genomes. *Molecular Biology of Chemosensory Receptors: The First Decade* (Peter Mombaerts and Stuart Firestein, March 11–14) was devoted to a review of all that is known of these molecules. In conjunction with this meeting, *Chemosensory Receptor Classification* (Peter Mombaerts, Stuart Firestein, and Randall Reed, March 15) was a workshop on possible approaches for classification of receptors and their families.

A meeting on *Mammalian Cloning: Biology and Practice* held at the Center in 2000 discussed technical aspects of the high failure rate of cloning. *Stability and Reversal of the Differentiated State* (Robin Lovell-Badge, David Stocum, and Jan Witkowski, October 28–31) concentrated on the biology that might underlie these failures, examining the fundamental biology of differentiation and its reversal. Participants worked on imprinting, X-inactivation, methylation, stem cells, germ cells, regeneration, and cloning in organisms as diverse as amphibia, mammals, and plants.

Epithelial and endothelial tubes are a fundamental structural unit of organ design, but very little is known about how epithelial and endothelial tubes form, how their sizes and shapes are regulated, and how tubular structures are maintained. *Epithelial and Endothelial Tube Morphogenesis* (Mark Krasnow and W. James Nelson, November 11–14) reviewed what is known from basic cell biological studies and genetic analysis of tube formation and maintenance in organisms as diverse as *C. elegans, Drosophila*, zebrafish, and mice, and the identification of genes involved in human tubulogenesis disorders.

The History and Mechanisms of Animal and Plant Evolution (John Doebley, Charles Marshall, and Nipam Patel, October 21–24) took on a big topic—how it is that plants and animals have come to be the way they are today. Participants included paleontologists, developmental biologists, geneticists, and morphologists. All were expected to contribute their own special knowledge to discussions of the relationship between micro- and macro-evolution, the early diversification of phyla, the genetic basis of evolutionary changes in morphology and development, and the adaptive forces underlying evolutionary change.

The theme of including animal and plant studies was continued in *Common and Contrasting Mechanisms of Pathogen Virulence and Host Resistance in Plant and Animal Diseases* (Jorge Galan and Brian Staskawicz, April 8–11). This discussion meeting brought together researchers working on microbial pathogenesis and host resistance mechanisms in both plant and animal systems. Researchers working on animal cells have advantages in cell biology and biochemistry, whereas the plant community has led in the genetic dissection of host response to pathogen infection. Key questions discussed included whether plant and animal pathogens share common mechanisms of pathogenesis and whether the signaling mechanisms involved are conserved between plant and animal hosts.

Neurological Disorders

The Fragile X syndrome is one of the best-characterized developmental genetic disorders, and rapid advances are being made in understanding the biological processes involved. *Understanding the Neural Basis of Fragile X* (William Greenough, David Nelson, and Don Bailey, March 4–7) reviewed the data coming from the wide range of studies on various aspects of basic and clinical research relating to the neural basis of Fragile X, including the nervous system phenotype in Fragile X syndrome and animal models, and FMRP synthesis, regulation, and the mRNAs to which it binds.

The other two meetings in this category discussed neurological disorders that are poorly characterized. Autism is a particularly controversial subject, especially in relation to its possible environmental causes. *Microbiology, Immunology, and Toxicology of Autism and Other Neurodevelopmental Disorders* (Ian Lipkin, February 11–14) tackled a broad range of topics relating to autism, including the genetics and neurobiology of autism, the general issue of the toxicology of neurodevelopmental disorders, and the possible role of vaccines as a cause of autism.

Another major neurological disorder that remains intractable is depression, and one area that has been especially neglected is childhood depression. Banbury took a small step to rectify this by holding a meeting on *Childhood Depression: A Critical Review* (Boris Birmaher and Ian Goodyer, February 20–23). First-episode depression occurs in the 8- to 18-year age group, and therefore this is an impor-



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tant group to study from an etiological as well as clinical perspective. The meeting examined features such as why it is that depressions are uncommon in prepubertal children compared to postpubertal adolescents, and why childhood depressives do not respond to antidepressants, whereas adolescent depressives do.

Workshop for Judges

Banbury Center has always had a strong interest in the public understanding of science, having had workshops for science journalists and congressional staff for many years. These have continued in the *Basic Issues of Science* workshops, held in conjunction with the Federal Judicial Center in Washington. The workshops do not deal with the role of science in the courtroom but rather introduce the concepts and styles of science to the judges. This was, as always, a delightful meeting, and one highlight was the presentation and discussion by Peter Neufeld, who established the Innocence Project with Barry Scheck. (Peter Neufeld first came to Banbury for the 1989 meeting on *DNA and Forensic Science*, a historic meeting that had an important role in the early debates about DNA fingerprinting.)

The American Eugenics Image Archive Project

This project, a collaborative effort with the Dolan DNA Learning Center, is proving to be a great success. In 2001, Dave Micklos and I implemented a further step in the project with a meeting *American Eugenics and the New Biology: Perspectives and Parallels* (David Micklos and Jan Witkowski, May 6–8). The meeting provided an opportunity for opinion leaders and policymakers from government, science, health care, education, and the mass media to learn about America's past involvement in eugenics from leading experts. As we had hoped, the eclectic mix of high-level participants and presenters created lively exchanges.

We also held a meeting of the Project's Eugenics Advisory Board (David Micklos and Jan Witkowski, September 30–October 1). This was a most important meeting in that the Board recommended to the National Institutes of Health that the site be made public in its entirety.

The Watson School of Biological Sciences—Topics in Biology

Banbury Center again held the week-long *Topics in Biology* course for students of The Watson School of Biological Sciences. This year the topic was evolution, and the lead instructor was Nipam Patel. The breadth of the course was great, running from reviewing the immense variety of life to the details of molecular evolution. A highlight of the week was a visit to the American Museum of Natural History.

Other Meetings

Several Laboratory groups came to Banbury for review and planning meetings, as did the Dolan DNA Learning Center and the Cold Spring Harbor Laboratory Press. As usual, we made the Center available to a small number of local community groups, notably Lloyd Harbor Village, The Cold Spring Harbor School District, and Holiday House.

Meier House

The Meier House was purchased by the Laboratory in 1999 to provide additional accommodation for Banbury Center meetings and to serve as a place where writers could come for periods of time to work in peace on their books. It has been an invaluable addition to the Banbury estate, and there is no doubt that participants in our meetings have enjoyed using it.

Funding

The sources of support for Banbury Center meetings are given for each meeting in the following list of programs. The Center and the scientists who participated in our meetings are very grateful for the generosity of all those institutions that provided this support.

Acknowledgments

Participants in Banbury Center meetings invariably make two comments. The first is on the beauty of the estate, and the second, on how well the meetings are organized. The praise belongs to the staff of the Center and the Laboratory. Bea Toliver, Ellie Sidorenko, and Katya Davey make sure that the meetings run properly, and Chris McEvoy, Andy Sauer, and Joe Ellis keep the estate looking beautiful. The staff of the Audiovisual Department helped the meetings run smoothly by dealing with the complexities of matching computers and PowerPoint. The Meetings Office works with us on the increasingly difficult task of interleaving the Grace Auditorium and Banbury Center meetings, and Housekeeping has looked after all the visitors for us. Finally, the Center could not work at all without the enthusiasm of its organizers and participants.

Jan Witkowski



Entrance to Banbury Center

MEETINGS

Microbiology, Immunology, and Toxicology of Autism and Other Neurodevelopmental Disorders

February 11–14

FUNDED BY	Cure Autism Now Foundation, McNeil Consumer Healthcare, National Alliance for
	Autism Research (NAAR), and the University of California, Davis M.I.N.D. Institute

ARRANGED BY W.I. Lipkin, University of California, Irvine

Introduction:

J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory W.I. Lipkin, University of California, Irvine

SESSION 1: Scope of the Problem: Epidemiology of Autism and Neurodevelopmental Disorders **Co-Chairpersons: G. Dawson,** University of Washington, Seattle and **J. Cordero,** Centers for Disease Control and Prevention, Atlanta, Georgia

- E. Susser, HIV Center for Clinical and Behavioral Studies, New York, New York: Epidemiological approaches to neurodevelopmental disorders.
- E. Fombonne, Institute of Psychiatry, King's College London, United Kingdom: Epidemiology of autism.
- B. Taylor, Royal Free & University College Medical School, London, United Kingdom: MMR in the UK and prevalence of

SESSION 2: Host Factors: Genetics of Autism Chairperson: E. London, National Alliance for Autism Research, Princeton, New Jersey

- C. Gilliam, Columbia Genome Center, New York, New York: Genetics of autism (AGRE Project).
- M.A. Pericak-Vance, Duke University Medical Center, Durham, North Carolina: Genetics.

- autism spectrum disorders.
- M. Yeargin-Allsopp, Centers for Disease Control and Prevention, Atlanta, Georgia: Past and future perspectives in autism epidemiology.
- J. Cordero, Centers for Disease Control and Prevention, Atlanta, Georgia: Review of epidemiology presentations.





E. Fombonne, E. Susser

SESSION 3: Anatomy and Neurobiology of Autism Chairperson: D.G. Amaral, University of California, Davis, Sacramento

- T.L. Kemper, Boston University School of Medicine, Massachusetts: Neuropathology of autism.
- N. Minshew, University of Pittsburgh Medical Center, Pennsylvania: Cortical dysfunction in autism.
- D.C. Chugani, Children's Hospital of Michigan, Detroit: Neuro-

SESSION 4: Immunology of Neurodevelopmental Disorders Chairperson: W.I. Lipkin, University of California, Irvine

- S.E. Swedo, National Institute of Mental Health, Bethesda, Maryland: PANDAS in OCD spectrum disorders.
- W.I. Lipkin, University of California, Irvine: A murine PANDAS model.
- E. Hollander, Mount Sinai School of Medicine, New York, New York: D8/17 and autism.

SESSION 5: Animal Models

Chairperson: S. Jacobson, National Institute of Neurological Disorders & Stroke, Bethesda, Maryland

- M. Hornig, University of California, Irvine: Infectious and immune factors in neurodevelopmental damage.
- K.M. Carbone, Food and Drug Administration, Bethesda, Maryland: Viral immune models of autism.

SESSION 6: Toxicology of Neurodevelopmental Disorders Chairperson: N. Minshew, University of Pittsburgh Medical Center, Pennsylvania

- M. Aschner, Wake Forest University School of Medicine, Winston-Salem, North Carolina: Neuropathogenesis of mercurv intoxication.
- S. Barone, Environmental Protection Agency, Research Triangle Park, North Carolina: Effects of gestational mercury

SESSION 7

- Co-Chairpersons: W.I. Lipkin, University of California, Irvine and E. Susser, HIV Center for Clinical and Behavioral Studies, New York, New York
- A.J. Wakefield, Royal Free & University College Medical School, London, United Kingdom: MMR, the gut, and autism.
- J. O'Leary, Coombe Women's Hospital, Dublin, Ireland: Molecular detection of measles virus sequences in white cells and gastrointestinal tissues of children with neurodevelopmental disorders.

chemical pathways in autism.

- G. Dawson, University of Washington, Seattle: Early indices of brain dysfunction in autism.
- E. Courchesne, University of California, San Diego, La Jolla: Functional and structural imaging studies in autism.
- S. Jacobson, National Institute of Neurological Disorders & Stroke, Bethesda, Maryland: Viral paradigms for chronic CNS diseases.
- K.B. Nelson, National Institute of Neurological Disorders & Stroke, Bethesda, Maryland: Neonatal predictors of neurodevelopmental disorders.

D.G. Amaral, University of California, Davis, Sacramento: The role of the amygdala in social behavior: Implications for autism.

L.R. Young, Emory University, Atlanta, Georgia: Social interactions in prairie voles.

exposure on neurotrophic factor signaling and altered development of the nervous system.

S. Bernard, ARC Research, Cranford, New Jersey: Mercury and autism pathogenesis.

M.A. Afzal, National Institute for Biological Standards & Control, Herts, United Kingdom: Vaccines, Crohns disease, and autism.

F. DeStefano, Centers for Disease Control & Prevention, Atlanta, Georgia: Review of vaccines and autism epidemioloav.

W.I. Lipkin, University of California, Irvine: Closing summary.





E. Hollander, S. Swedo, B. Taylor

Childhood Depression: A Critical Review

February 20-23

FUNDED BY	Cold Spring Harbor Laboratory	

ARRANGED BY B. Birmaher, University of Pittsburgh Medical Center, Pennsylvania I.M. Goodyer, University of Cambridge, United Kingdom

Introduction:

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

SESSION 1: Conceptual Aspects

Chairperson: I.M. Goodyer, University of Cambridge, United Kingdom

- S.J. Suomi, National Institute of Child Health and Human Development, Bethesda, Maryland: Childhood depression: A critical review.
- R. Hornsby, Sir Robert Mond Memorial Trust, London, United Kingdom: A personal perspective (on adolescent despair).

evolutionary psychology of depression.

L. Wolpert, University College London, United Kingdom: The

SESSION 2: Clinical Aspects

- Co-Chairpersons: I.M. Goodyer, University of Cambridge, United Kingdom and L. Wolpert, University College London, United Kingdom
- J. Kaufman, Yale University, New Haven, Connecticut: Are child-, adolescent-, and adult-onset depression one and the same disorder?
- P.J. Ambrosini, MCP-Hahnemann University, Philadelphia,
- Pennsylvania: Irritability in adolescent affective disorders.
- E. Fombonne, King's College London, United Kingdom: Longterm outcomes of child and adolescent depression: The Maudsley study.



I. Goodyer, L. Wolpert, J. Costello

SESSION 3: Biological Studies

Chairperson: L. Wolpert, University College London, United Kingdom

- A.C. Angold, Duke University Medical Center, Durham, North Carolina: The roles of various types of stressor, parental depression, testosterone, and estradiol in relation to changing rates of depression.
- J.A. Graber, Columbia University, New York, New York: Psycho-

SESSION 4: Social Environment Influences

Chairperson: B. Birmaher, University of Pittsburgh Medical Center, Pennsylvania

- J. Costello, Duke University, Durham, North Carolina: Child and adolescent depression: Prodromal signs and symptoms.
- J. Garber, Vanderbilt University, Nashville, Tennessee: Psychosocial predictors of depression in adolescents.
- M.A. Rueter, University of Minnesota, St. Paul: Familial influ-

SESSION 5: Affective-Cognitive Processes

Co-Chairpersons: B. Birmaher, University of Pittsburgh Medical Center, Pennsylvania and E. Fombonne, King's College London, United Kingdom

- L. Murray, University of Reading, United Kingdom: Identifying cognitive vulnerability to depression in five-year-olds.
- I. M. Goodyer, University of Cambridge, United Kingdom: Are sensitive minds bad for the brain? Mood-linked cognitions as

SESSION 6: Pharmacological Treatment

Chairperson: E. Fombonne, King's College London, United Kingdom

N. Ryan, University of Pittsburgh Medical Center, Pennsylvania: SSRIs treat child and adolescent major depression while TCAs are ineffective: Is this a real difference in noradrenergic versus serotonergic therapeutic strategies or is it merely an

SESSION 7: Family/Genetic Approaches

Chairperson: S.J. Suomi, National Institute of Child Health and Human Development, Bethesda, Maryland

R.D. Todd, Washington University School of Medicine, St. Louis, Missouri: Gene-environment interactions in the development of early-onset depression: Results from an epidemiologically based twin study of brain morphometry.

SESSION 8: Neuroimaging

Chairperson: S.J. Suomi, National Institute of Child Health and Human Development, Bethesda, Maryland

- H. Blumberg, Yale University, New Haven, Connecticut: Structural and functional MRI studies of bipolar disorder in adolescents and adults.
- K.N. Botteron, Washington University School of Medicine,

social predictors of depression in adolescents.

- B. Birmaher, University of Pittsburgh Medical Center, Pennsylvania: Biological studies in never depressed children at high risk to develop MDD.
- ences on early (prepubertal) versus later (postpubertal) first onset of MDE.
- D. Williamson, University of Pittsburgh Medical Center, Pennsylvania: Environmental risk factors for depression in children and adolescents.

psychoendocrine insults.

L. Mufson, New York State Psychiatric Institute, New York: IPT-A: Translating efficacy into effectiveness research.

R.A. Kowatch, University of Cincinnati Medical Center, Ohio:

Pharmacological trials in pediatric bipolars: Is placebo necessary?

artifact of available studies?

Children and depression: Results from top-down and bottom-up studies.

M.M. Weissman, Columbia University, New York, New York:

St. Louis, Missouri: Structural brain differences in early-onset depression: Neurodevelopmental or neurodegenerative mechanisms.

Integrating Genomics Technologies in Health Care: Practice and Policy Challenges

February 25-28

FUNDED BY Burroughs Wellcome Fund, Hoffmann-La Roche Inc., and Affymetrix, Inc.

ARRANGED BY M.J.F. Austin, Hoffmann-La Roche Inc., Nutley, New Jersey T. Kreiner, Affymetrix, Inc., Santa Clara, California

Introduction:

J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory M.J.F. Austin, Hoffmann-La Roche Inc., Nutley, New Jersey

SESSION 1: Technologies and Analysis Chairperson: L. Babiss, Hoffmann-La Roche Inc., Nutley, New Jersey

- J. Warrington, Affymetrix, Inc., Santa Clara, California: Microarray applications in diagnostics.
- W.H. Koch, Roche Molecular Systems, Alameda, California: Microarray-based genotyping of polymorphic drug metabolism: Pharmacogenetics lessons galore.
- E. Lai, Glaxo Wellcome Inc., Research Triangle Park, North Carolina: Application of SNP technologies in health care: What have we learned and what are the challenges?

SESSION 2: Applications I

Chairperson: U. Francke, HHMI, Stanford University Medical Center, California

- N.C. Dracopoli, Bristol-Myers Squibb, Princeton, New Jersey: Application of pharmacogenomics in clinical drug development.
- C. Dykes, Variagenics, Inc., Cambridge, Massachusetts: Candidate gene studies within clinical development.
- N.A. Holtzman, The Johns Hopkins Medical Institutions, Baltimore, Maryland: Separating genotype from genohype: Will we be able to predict and prevent common com-

E.S. Winn-Deen, Celera Genomics, Rockville, Maryland: Diagnostics in the postgenomic era.

- J. Hoh, Rockefeller University, New York, New York: Problems in the analysis of microarray data from first principles.
- J.D. Terwilliger, Columbia University, New York, New York: Why the HGP will likely have minimal if any effect on public health and medicine in the foreseeable future.

plex diseases?

- B.R. Korf, Partners Center for Human Genetics and Harvard Medical School, Boston, Massachusetts: Integration of genetics into medical practice.
- D.K. Burns, Glaxo Wellcome Inc., Research Triangle Park, North Carolina: Moving genetics from research to impacting clinical practice: The GlaxoSmithKline perspective.



M. Austin, D. Burns, E. Winn-Deen

SESSION 3: Applications II

Chairperson: U. Francke, HHMI, Stanford University Medical Center, California

- A. Guttmacher, National Human Genome Research Institute, Bethesda, Maryland: From research laboratory to neighborhood health center: The NHGRI's efforts to translate DNA into health care.
- C.C. Morton, Brigham & Women's Hospital, Boston, Massachusetts: Genomic resources applied in the clinical cytogenetics laboratory.
- W. Uhlmann, University of Michigan, Ann Arbor: Genetic counseling in our current health care system.G. Wiesner, Case Western Reserve University, Cleveland, Ohio:
- The GREAT system: Linking genomics to primary care.
- R.L. White, DNA Sciences, Inc., Fremont, California: DNA Sciences' Gene Trust Project.

SESSION 4: Regulatory and Policy Issues **Chairperson: L. Knowles,** The Hastings Center, Garrison, New York

- G. Koski, National Institutes of Health, Rockville, Maryland: Realism and regulation of research in the genomics era.
- P.F. Terry, Genetic Alliance, Washington, D.C.: Policy issues: A consumer perspective.
- B. Koenig, Stanford University, California: Update on the Secretary's Advisory Committee on Genetic Testing (SACGT);
- Identifying "Race": Looking through a genomics prism.
- J. Doll, U.S. Patent and Trademark Office, Arlington, Virginia: The ground rules for genomic patenting.
- H.T. Greely, Stanford University Law School, California: Regulatory and health financing constraints on clinical genomics.
- SESSION 5: Closing Discussion: Managing the Future—A Group Discussion to Identify Key Needs and Next Steps
- Interlocutors: T. Kreiner, Affymetrix, Inc., Santa Clara, California and M.J.F. Austin, Hoffmann-La Roche Inc.
- L. Babiss, Hoffmann-La Roche Inc., Nutley, New Jersey: Technology and analysis key trends.
- U. Francke, HHMI, Stanford University Medical Center,
- California: Applications and clinical applications key trends. L. Knowles, The Hastings Center, Garrison, New York: Regulatory and policy issues.



Meeting in session.

Understanding the Neural Basis of Fragile X

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FUNDED BY	National Institute of Mental Health (NIMH), with additional support from National Institute of Child Health and Human Development (NICHD) (through a grant to the University of Illinois, Urbana)
ARRANGED BY	W. Greenough, University of Illinois, Urbana D.L. Nelson, Baylor College of Medicine, Houston, Texas D. Bailey, University of North Carolina at Chapel Hill

Introduction:

J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory K. Clapp, FRAXA Research Foundation, Newburyport, Massachusetts

SESSION 1: Human Phenotype

Chairperson: L. Crnic, University of Colorado Health Sciences Center, Denver

- R.J. Hagerman, MIND Institute, University of California, Davis Medical Center, Sacramento: Spectrum of involvement in Fragile X syndrome and in permutation area.
- D. Bailey, University of North Carolina, Chapel Hill: Opportunities for integrative biobehavioral research in Fragile

SESSION 2: Animal Phenotype

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

- W.T. Greenough, University of Illinois, Urbana: FMRP expression and neural morphology.
- W.T. Brown, New York State Institute for Basic Research, Staten Island: Toward an improved mouse model of Fragile X.
- B. Oostra, Erasmus Universiteit Rotterdam, The Netherlands: Mouse models for Fragile X syndrome.
- L. Crnic, University of Colorado Health Sciences Center, Denver: Abnormalities in the auditory startle response in

X syndrome.

E. Berry-Kravis, Rush Children's Hospital, Chicago, Illinois: Pharmacological approaches to seizures, behavior, and cognition in Fragile X syndrome: Present and future.

FMR1-targeted mutants on several genetic backgrounds.

- R.E. Paylor, Baylor College of Medicine, Houston, Texas: More behavioral phenotyping of mouse models of Fragile X.
- H. Siomi, University of Tokushima, Japan: Cell culture and whole animal approaches to understanding the function of the FMR1 protein in *Drosophila*.
- J.R. Larson, University of Illinois, Chicago: Olfactory learning and memory in mice.



K. Clapp, W. Greenough

SESSION 3: FMR1 mRNA Transport, Regulation of FMRP Synthesis, and Interacting Proteins

Chairperson: W.T. Greenough, University of Illinois, Urbana

- D.L. Nelson, Baylor College of Medicine, Houston, Texas: Consequences of mutation of the *FMR1/FXR* genes in mouse and fly.
- G.J. Bassell, Albert Einstein University, Bronx, New York: FMRP trafficking in cultured hippocampal neurons.
- G. Neri, Universita Cattolica, Rome, Italy: Pharmacological reactivation of the fully mutated *FMR1* gene.
- P. Chiurazzi, Universita Cattolica, Rome, Italy: Methylation analysis of the promoter of the inactive and reactivated fully mutated *FMR1* gene.
- P.J. Hagerman, University of California, Davis: Expression of the Fragile X gene.
- K.M. Huber, Brown University, Providence, Rhode Island: Role

SESSION 4: Cellular Functions of FMRP

Chairperson: D.L. Nelson, Baylor College of Medicine, Houston, Texas

I.J. Weiler, University of Illinois, Urbana-Champaign: Some translational deficits in Fmr-1 knockout.

SESSION 5: Interacting RNAs and Proteins **Chairperson: P.J. Hagerman,** University of California, Davis

- B. Bardoni, CNRS, Illkirch, France: Search for FMRP function through the characterization of four novel FMRP-interacting proteins.
- H. Moine, CNRS, Strasbourg, France: Characterization of a specific binding target for FMRP on its own mRNA.
- J. Darnell, Rockefeller University, New York, New York: Identification of sequence-specific RNA targets for KH2 and

for dendritic protein synthesis in hippocampal long-term depression.

- K.J. Mack, University of Wisconsin, Madison: Sensory experience increases, and seizures reduce, expression of the Fragile X mental retardation protein.
- R.P. Bauchwitz, St. Luke's-Roosevelt Institute of Health Sciences, New York: Further analysis of Fmr1 transgenic and knockout mice.
- R.F. Kooy, University of Antwerp, Belgium: Differentially expressed sequences in the Fragile X knockout mouse.
- S.T. Warren, Emory University School of Medicine, Atlanta, Georgia: DNA chip analysis of FMRP function and the consequence of its absence.
- M.C. Rattazzi, New York State Institute for Basic Research, Staten Island: Toward gene therapy of Fragile X syndrome.

newly characterized high-affinity RNA-binding domains of FMRP.

A.T. Hoogeveen, Erasmus University Medical School, Rotterdam, The Netherlands: FMRP and its related proteins.

E.W. Khandjian, Hop. St. Francois d'Assise, Quebec, Canada: The expanding Fragile X protein family: RNA-binding proteins and more?



Coffee break on back porch of Banbury Conference Center.

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Molecular Biology of Chemosensory Receptors: The First Decade

March 11–14

FUNDED BY	Cold Spring Harbor Laboratory Corporate Sponsor Program,
	with additional support from Senomyx, Inc.

ARRANGED BY P. Mombaerts, The Rockefeller University, New York, New York S. Firestein, Columbia University, New York, New York

Introduction:

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

Opening Lecture:

L.B. Buck, Harvard Medical School, Boston, Massachusetts

SESSION 1: Mammalian Odorant Receptors: Genomics Chairperson: P. Mombaerts, The Rockefeller University, New York, New York

- D. Lancet, Weizmann Institute of Science, Rehovot, Israel: Mining the genome: The complete human olfactory receptor repertoire.
- S. Zozulya, Senomyx, Inc., La Jolla, California: The repertoire of human functional odorant receptor candidates.
- B.J. Trask, Fred Hutchinson Cancer Research Center, Seattle,

SESSION 2: Other Chemosensory Receptors Chairperson: R. Axel, HHMI, Columbia University, New York, New York

- R. Tirindelli, Universita di Parma, Italy: The coexpression of putative pheromone receptors suggests another mode of information processing in the olfactory systems.
- L. Vosshall, The Rockefeller University, New York, New York: Determinants of spatial convergence in the *Drosophila* olfactory system.
- H. Amrein, Duke University Medical Center, Durham, North Carolina: Identification and expression of a large family of

Washington: Comparative OR genomics: Large-scale change and polymorphism.

- J. Strotmann, University of Hohenheim, Stuttgart, Germany: Olfactory receptors with atypical features.
- S. Firestein, Columbia University, New York, New York: Molecular pharmacology of odor receptors.

Drosophila taste receptor genes.

- C.I. Bargmann, University of California, San Francisco: Odor discrimination and olfactory receptor expression in *C. elegans*.
- H. Robertson, University of Illinois at Urbana-Champaign: Molecular evolution of the nematode and insect chemoreceptor superfamilies.



L. Buck, R. Axel, N. Ryba

SESSION 3: Taste Receptors

Chairperson: M. Zoller, Senomyx, Inc., La Jolla, California

- J.F. Battey, National Institute on Deafness and Other Communication Disorders, Bethesda, Maryland: Discovery of genes selectively expressed in taste receptor cells.
- N. Ryba, National Institute of Dental and Craniofacial

SESSION 4: Odorant Receptors: Molecular Biology

Chairperson: R.F. Margolskee, HHMI, Mount Sinai School of Medicine, New York, New York

- A. Chess, Whitehead Institute, Cambridge, Massachusetts: Genome-wide coordination of olfactory receptor genes.
- T. McClintock, University of Kentucky, Lexington: Intracellular trafficking of olfactory receptors.

SESSION 5: Odorant Receptors: Development Chairperson: L.B. Buck, Harvard Medical School, Boston, Massachusetts

- B. Key, University of Queensland, Brisbane, Australia: Changing the cell surface glycocode on olfactory axons via transgenesis: The combined role of odorant receptors and cell surface.
- C.A. Greer, Yale University School of Medicine, New Haven, Connecticut: Axonal targeting and organization of the olfac-

tory bulb glomerulus.

1990-2000.

- R.R. Reed, HHMI, The Johns Hopkins University, Bethesda, Maryland: Engineering altered activity in the mammalian olfactory system.
- H. Sakano, University of Tokyo, Japan: Mutually exclusive expression of odorant receptor transgenes.

SESSION 6: Odorant Receptors: Function

Chairperson: S. Firestein, Columbia University, New York, New York

- G.M. Shepherd, Yale University Medical School, New Haven, Connecticut: Odor determinants, receptor-binding pockets, and odor images: Convergence of experiment and theory.
- C. Wetzel, Ruhr-University-Bochum, Germany: Functional expression and characterization of olfactory receptors of vertebrates and invertebrates.
- D. Giorgi, Institut de Genetique Humaine, Montpellier, France:

Closing Lecture:

R. Axel, HHMI, Columbia University, New York, New York

Identification of specific ligands of mouse OR912-93.

- S. Korsching, University of Cologne, Germany: Concentration and structure-dependent odor space in the mouse olfactory bulb.
- K. Touhara, University of Tokyo, Japan: Reconstitution of mouse olfactory receptors that recognize an overlapping set of odorants.

Research, Bethesda, Maryland: Bitter taste receptors. N. Chaudhari, University of Miami School of Medicine, Florida: Comparing *umami* taste with the properties of a cloned taste receptor.

B. Davis, National Institute on Deafness and Other Communication Disorders, Rockville, Maryland: The

growth and the taste and smell programs at the NIDCD,

Genomic Annotation Workshop: DNA Replication

March 17-22

FUNDED BY National Institutes of Health

ARRANGED BY L.D. Stein, Cold Spring Harbor Laboratory E. Birney, European Bioinformatics Institute, Cambridge,United Kingdom

WORKSHOP MEMBERS:

L.I. Aravind, National Center for Biotechnology Information, National Library of Medicine (NLM), Bethesda, Maryland J. Ashurst, Sanger Centre, Cambridge, United Kingdom

A.G. Bateman, Sanger Centre, Cambridge, United Kingdom

E. Birney, European Bioinformatics Institute, Cambridge, United Kingdom

M. Clamp, Sanger Centre, Cambridge, United Kingdom

R. Copley, EMBL Heidelberg, Germany

E.E. Eichler, Case Western Reserve University, Cleveland, Ohio

J. Gilbert, Sanger Centre, Cambridge, United Kingdom

A. Kanapin, European Bioinformatics Institute, Cambridge, United Kingdom

A. Neuwald, Cold Spring Harbor Laboratory

K. Pruitt, National Library of Medicine (NLM), Bethesda, Maryland

- J. Stalker, Sanger Centre, Cambridge, United Kingdom
- L.D. Stein, Cold Spring Harbor Laboratory
- B. Stillman, Cold Spring Harbor Laboratory
- E. Stupka, European Bioinformatics Institute, Cambridge, United Kingdom



Bioinformaticists at work.

The Basic Issues of Science

April 1-4

FUNDED BY The Federal Judicial Center

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

SESSION 1

SESSION 4

- J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory and F.M. Smith, Federal Judicial Center, Washington, D.C.: Welcoming remarks.
- G.E. Allen, Washington University, St. Louis, Missouri: Eugenics: Past, present, and future.

SESSION 2

- J. Maienschein, Arizona State University, Tempe: From Darwin to Dolly: Developments in the biological sciences in the 20th century.
- J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory: Fundamentals of genetics.

SESSION 3

- J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory: The Human Genome Project: Origins and future.
- D. Blacker, Massachusetts General Hospital, Boston, Massachusetts: Using molecular human genetics: Alzheimer's disease.

P. Reilly, Interleukin Genetics, Inc., Waltham, Massachusetts: Social implications of genetic research.

SESSION 5

P. Neufeld, Innocence Project, New York, New York: Using DNA forensics.

SESSION 6

- I. Pepperberg, Massachusetts Institute of Technology, Cambridge, Massachusetts: What Alex the Grey Parrot tells us about human cognition and language.
- R. Park, University of Maryland, College Park, Maryland: Science and pseudoscience and the courtroom.



Federal Judicial Conference attendees.

Common and Contrasting Mechanisms of Pathogen Virulence and Host Resistance in Plant and Animal Diseases

April 8–11

FUNDED BY	Cold Spring Harbor Laboratory Corporate Sponsor Program
ARRANGED BY	J. Galan, Yale University School of Medicine, New Haven, Connecticut B.J. Staskawicz, University of California, Berkeley
Introductions	

Introduction:

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

SESSION 1: Innate Immunity and Host Defense Responses **Chairperson: B.J. Staskawicz,** University of California, Berkeley

- K. Anderson, Memorial Sloan-Kettering Institute, New York, New York: Genetic analysis of the response to infection in *Drosophila*.
- G. Nunez, University of Michigan Medical School, Ann Arbor: Regulation of apoptosis and NF- κB activation by Nod proteins.
- S. Miller, University of Washington, Seattle: Lipid A modifications and the resistance of gram-negative bacteria to innate immunity.

SESSION 2: Bacterial Modulators of Host Responses

- Chairperson: J. Galan, Yale University School of Medicine, New Haven, Connecticut
- J. Galan, Yale University School of Medicine, New Haven, Connecticut: Mimicry of cellular proteins as a strategy for the modulation of cellular responses by bacterial pathogens.
- H. Wolf-Watz, University of Umea, Sweden: Modulation of expression and translocation of *Yersinia* virulence effectors after target cell contact.
- D. Philpott, Institut Pasteur, Paris, France: How *Shigella* plants the seeds of inflammation into intestinal cells.

K. Orth, University of Michigan Medical Center, Ann Arbor:

- B.J. Staskawicz, University of California, Berkeley: NDR1, a putative GPI-anchored protein specifying bacterial disease resistance in *Arabidopsis thaliana*.
- J. Parker, The Sainsbury Laboratory, Norwich, United Kingdom: Connecting local and systemic plant resistance pathways.
- X. Dong, Duke University, Durham, North Carolina: Signal transduction in systemic acquired resistance.

Black death, Black spot: Yersinia effector is a ubiquitin-like protein protease.

- A. Collmer, Cornell University, Ithaca, New York: The Hrp (type III secretion system) effector proteins of *Pseudomonas syringae* pv. tomato DC3000.
- U. Bonas, Martin-Luther University, Halle, Germany: Type III effector proteins and their role in the *Xanthomonas*-plant interaction: Recognition or disease?



U. Bonas, J. Dangl, B. Staskawicz, P. Schulze-Lefert

SESSION 3: Mechanisms of Microbial/Host Interactions I Chairperson: D. Portnoy, University of California, Berkeley

- G.B. Martin, Cornell University, Ithaca, New York: *Pseudo-monas* effector proteins that interact with the tomato Pto kinase.
- J. Dangl, University of North Carolina, Chapel Hill: Type III effectors in the *P. syringae* interaction with *Arabidopsis*.
- R. Innes, Indiana University, Bloomington: Recognition of the *Pseudomonas* virulence protein AvrPphB by *Arabidopsis*.
- D. Portnoy, University of California, Berkeley: A PEST-like se-

SESSION 4: Mechanisms of Microbial/Host Interactions II Chairperson: J.D.G. Jones, The Sainsbury Laboratory, Norwich, United Kingdom

- J.D.G. Jones, The Sainsbury Laboratory, Norwich, United Kingdom: Mode of action of tomato Cf- genes that confer resistance to *Cladosporium fulvum*.
- J. Ellis, CSIRO, Canberra, Australia: Specificity, repression, and activation of rust resistance proteins.
- S. Hulbert, Kansas State University, Manhattan: NBS genes in cereals.
- K. Shirasu, The Sainsbury Laboratory, Norwich, United King-

SESSION 5: Plant Defense Responses

Chairperson: F.M. Ausubel, Massachusetts General Hospital, Boston

P. Schulze-Lefert, Max-Planck-Institut für Zuchtungsforschtung, Koln, Germany: Activation of and rescue from cell death in plant disease resistance.

SESSION 6: Model Systems and Genomics

Chairperson: F.M. Ausubel, Massachusetts General Hospital, Boston

F.M. Ausubel, Massachusetts General Hospital, Boston: Modeling human pathogenesis in nonvertebrate model hosts.P.F. Predki, DOE Genome Institute, Walnut Creek, California: Rapid characterization of pathogen genomes via highthroughput draft sequencing.

S. Lory, Harvard Medical School, Boston, Massachusetts: Eavesdropping on communications between pathogens and their host using DNA microarrays.



J. Galan, E. Groisman, C. Roy

quence in listeriolysin O essential for *Listeria monocytogenes* pathogenicity.

- J.F. Miller, University of California, Los Angeles: Parasite adaptation to a dynamic host: *Bordetella*-phage interactions.
- S. Hultgren, Washington University, St. Louis, Missouri: Pathogenic fiber formation in bacteria: Structure, function, and role in diseases of the urinary tract.
- dom: RAR1: A link from R genes to ubiquitination machinery. C. Roy, Yale School of Medicine, New Haven, Connecticut: Implications for pathogen evolution: Hijacking of a eukaryotic host gene by *Legionella pneumophila*.
- E. Groisman, Washington University School of Medicine, St. Louis, Missouri: The SPI-2 pathogenicity island of *Salmonella* enteric.
- B. Baker, University of California, Berkeley: Molecular-genetic characterization of the N-mediated TMV disease resistance pathway.

Electronic Access to Scientific Literature

April 16-18

FUNDED BY Cold Spring Harbor Laboratory

ARRANGED BY J. Inglis, Cold Spring Harbor Laboratory Press J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory

Introduction:

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

J. Inglis, Cold Spring Harbor Laboratory Press

SESSION 1: Users' Wants and Needs

- Chairperson: B. Alberts, National Academy of Sciences, Washington, D.C.
- B. Stillman, Cold Spring Harbor Laboratory: What do scientists want? (followed by additional comments, participating scientists)
- A. Okerson, Yale University, New Haven, Connecticut: What do libraries want?

Additional comments, participating librarians.



B. Alberts, J. Sack, J. Fox, N. Cozzarelli



M. Eisen

SESSION 2: Cross-Publisher Initiatives

- Co-Chairpersons: B. Alberts, National Academy of Sciences, Washington, D.C. and N. Cozzarelli, PNAS-University of California, Berkeley
- D. Lipman, National Center for Biotechnology Information, NIH, Bethesda, Maryland: PubMed Central

Discussion of PubMed Central

K. Hunter, Elsevier Science, New York, New York: CrossRef

SESSION 3: What Are Individual Publishers Doing? **Chairperson: P. Campbell,** Nature Publishing Group, London, United Kingdom

Brief presentations and discussions by publishers.

SESSION 4: What Next?

Co-Chairpersons: J. Inglis, Cold Spring Harbor Laboratory Press and **J.A. Witkowski,** Banbury Center, Cold Spring Harbor Laboratory



R. Bovenshulte, K. Hunter

Interferons: Biological Mechanisms and Disease Treatments I

April 29-May 1

FUNDED BY Herbert J. Siegel Fund for Cancer Pharmacogenomics

ARRANGED BY I.J. Fidler, M.D. Anderson Cancer Center, Houston, Texas

Introduction:

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

SESSION 1

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

- I.J. Fidler, M.D. Anderson Cancer Center, Houston, Texas: Introduction and antiangiogenic properties of interferon α/β.
- J.E. Darnell, The Rockefeller University, New York, New York: The stats in cancer.
- B.B. Aggarwal, M.D. Anderson Cancer Center, Houston, Texas: Molecular basis for the antiproliferative and antiinflammatory effects of interferon.
- J.M. Folkman, Children's Hospital, Boston, Massachusetts: Antiangiogenic therapy with low-dose interferon α .

SESSION 2

- Chairperson: E.C. Borden, Cleveland Clinic Foundation, Taussig Cancer Center, Ohio
- C.P.N. Dinney, M.D. Anderson Cancer Center, Houston, Texas: Interferon gene therapy for superficial bladder cancer.
- J.M. Kirkwood, University of Pittsburgh Cancer Institute, Pennsylvania: Adjuvant therapy.
- A.M.M. Eggermont, University Hospital Rotterdam, The Netherlands: Adjuvant therapy with intermediate doses of IFN and the rationale of the Peg-Intron Eortc 18991 trial.
- B. Clarkson, Memorial Sloan-Kettering Cancer Center, New York, New York: New inhibitors of *abl* tyrosine kinase and other targets for specific therapies of CML.
- S. Rich, Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illinois: The role of growth factors and inhibitors in the pathobiology of primary pulmonary hypertension.

SESSION 3

- Chairperson: I.J. Fidler, M.D. Anderson Cancer Center, Houston, Texas
- E.C. Borden, Cleveland Clinic Foundation, Taussig Cancer Center, Ohio: Genes, apoptosis, and angiogenesis.
- P.B. Chapman, Memorial Sloan-Kettering Cancer Center, New York, New York: Utility of high-dose IFNα in melanoma.
- F. Randazzo, Chiron Corporation, Emeryville, California: Analyzing pathways in cancer by combining functional analysis with gene expression profiling of small tumor biopsy samples.
- S. Lowe, Cold Spring Harbor Laboratory: Cellular senescence induced by oncogenic *ras*.
- S.E. Krown, Memorial Sloan-Kettering Cancer Center, New York: Interferon therapy for Kaposi's sarcoma: Evidence for activity of low-dose daily interferon.



P. Chapman, E. Bergsland



I.J. Fidler, J. Folkman

American Eugenics and the New Biology: Perspectives and Parallels

May 6-8

FUNDED BY National Human Genome Research Institute, National Institutes of Health

ARRANGED BY D. Micklos, DNA Learning Center, Cold Spring Harbor Laboratory J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory

SESSION 1: History

G.E. Allen, Washington University, St. Louis, Missouri: Progressive origins of eugenics and the Eugenics Record Office.

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

SESSION 2: Impacts

- S. Selden, University of Maryland, College Park: Fitter families for future firesides: State fairs and the construction of merit and race in America, 1913–1930.
- P.A. Lombardo, University of Virginia, Charlottesville: Immigration and sterilization in the United States.
- N.A. Holtzman, The John Hopkins Medical Institutions, Baltimore, Maryland: Is eugenics dead and buried?

SESSION 3: Resources

D. Micklos, DNA Learning Center, Cold Spring Harbor and J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory: Introduction to the image archive on the American eugenics movement.



- D. Paul, Brandeis University, Waltham, Massachusetts: Comparative eugenics.
- D. Hamer, National Cancer Institute, Bethesda, Maryland: Genetics of human behavior.

Session 5: General Discussion



J. Apple, P. Seawell



G. Allen, N. Holtzman, P. Woolf

Can a Machine Be Conscious?

May 13-16

FUNDED BY	The Swartz Foundation
ARRANGED BY	 C. Koch, California Institute of Technology, Pasadena D. Chalmers, University of Arizona R. Goodman, California Institute of Technology, Pasadena O. Holland, Clinton House, Stroud, United Kingdom J. Swartz, The Swartz Foundation, East Setauket, New York

Introduction and Welcome:

J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory J. Swartz, The Swartz Foundation, East Setauket, New York

SESSION 1

Chairperson: C. Koch, California Institute of Technology, Pasadena

- D.J. Chalmers, University of Arizona, Tucson: Machine consciousness: Problems and prospects.
- C. Koch, California Institute of Technology, Pasadena: From biological to machine consciousness.
- G. Tononi, University of Wisconsin, Madison: Recipes for consciousness.
- E. Rolls, University of Oxford, United Kingdom: Consciousness and dual routes to action in neural network machines.

SESSION 2

Chairperson: R.M. Goodman, California Institute of Technology, Pasadena

- M.A. Goodale, University of Western Ontario, Canada: Why we need two cortical visual systems: A teleassistance model.
- C.D. Frith, University College London, United Kingdom: The importance of other minds.
- L. Steels, Free University of Brussels, Belgium: The role of language in the emergence of consciousness.
- J.C. Hawkins, Handspring Inc., Mountain View, California: What neuroanatomy and the physiology of our senses tell us about consciousness and intelligence.
- S. Blackmore, University of the West of England, Bristol, United Kingdom: Consciousness in meme machines.



C. Koch, A. Zador, J. Hawkins

SESSION 3

Chairperson: D.J. Chalmers, University of Arizona, Tucson

- N. Block, New York University Faculty of Arts & Sciences, New York: What are experiments about consciousness really about?
- E. Dietrich, Virginia Institute of Technology, Blacksburg: Can a machine be conscious? Sure, but it won't help.
- I. Aleksander, Imperial College, London, United Kingdom:

SESSION 4

Chairperson: O. Holland, Clinton House, Stroud, United Kingdom

- B. Baars, The Neurosciences Institute, San Diego, California: Self systems in the brain constrain conscious contents: A global workspace perspective.
- S. Franklin, University of Memphis, Tennessee: Conscious software agents. We've got one running. How conscious is it? I don't know.
- S. Dehaene, Service Hospitalier Frederic Joliot, Orsay, France:

SESSION 5

Chairperson: C. Koch, California Institute of Technology, Pasadena

D. Psaltis, California Institute of Technology, Pasadena: Awareness-based computing. Robot usable models of visual consciousness.

R.M. Goodman, California Institute of Technology, Pasadena and O. Holland, Clinton House, Stroud, United Kingdom: Autonomous robots + dynamic environment + intelligent control = consciousness?

Cerebral processing of conscious and unconscious stimuli: A neural workspace hypothesis.

- A.J. Clark, University of Sussex, Brighton, United Kingdom: Consciousness and perceptual knowledge.
- A. Cleeremans, Free University of Brussels, Belgium: Being virtual: Consciousness and self as graded, adaptive phenomena.



I. Aleksander, J. Witkowski

Interferons: Biological Mechanisms and Disease Treatments II

September 9–11

FUNDED BY Herbert J. Siegel Fund for Cancer Pharmacogenomics

ARRANGED BY E.C. Borden, Cleveland Clinic Foundation, Ohio J. Folkman, Children's Hospital, Boston, Massachusetts

Introductions:

J.D. Watson, Cold Spring Harbor Laboratory

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

SESSION 1: OFMs: Mechanisms and Antiangiogenic Effects Chairperson: I.J. Fidler, M.D. Anderson Cancer Center, Houston, Texas

- J. Folkman, Children's Hospital, Boston, Massachusetts: Introduction: IFNs overview of antiangiogenesis results.
- E.C. Borden, Cleveland Clinic Foundation, Ohio: Objective and the interferon system.
- I.J. Fidler, M.D. Anderson Cancer Center, Houston, Texas: INFNs: Preclinical antiangiogenesis mechanisms.

SESSION 2: Considerations in Clinical Study Designs Chairperson: E.C. Borden, Cleveland Clinic Foundation, Ohio

- S. Weiss, Emory University Hospital, Atlanta, Georgia: Pathology of angiogenic neoplasms.
- D. Lindner, Cleveland Clinic Foundation, Ohio: IFNs in preclinical tumor models.
- S.E. Krown, Memorial Sloan-Kettering Cancer Center, New York, New York: Effective dose and schedule for Kaposi's sarcoma.
- A.M.M. Eggermont, University Hospital Rotterdam, The Netherlands: Doses and schedules in melanoma—European experience.
- B.R.G. Williams, Cleveland Clinic Foundation, Ohio: Assessment of mechanisms by gene array.
- R. Kalluri, Beth Israel Deaconess Medical Center, Boston, Massachusetts: Tumstatin and INFN- α gene expression.
- J.M. Pluda, CTEP National Cancer Institute, Rockville, Maryland: Potential for combination with other antiangiogenic agents.
- **SESSION 3:** Discussion and Presentation of Preclinical and Phase II/III Cooperative Group Clinical Study Designs

Discussion Groups:

- A. Ezekowitz, Massachusetts General Hospital, Boston: Hemangiomas.
- A.W. Bleyer, University of Texas, M.D. Anderson Cancer Center, Houston: Giant cell tumors of bone.
- G. Thomas Budd, Cleveland Clinic Foundation, Ohio: Angiosarcomas.
- J.E. Darnell, The Rockefeller University, New York, New York: Critical preclinical questions.

Recommendations for Future Studies:

Co-Chairpersons: E.C. Borden, Cleveland Clinic Foundation, Ohio and **J. Folkman,** Children's Hospital, Boston, Massachusetts: Next steps and summary. J.E. Darnell, The Rockefeller University, New York, New York: IFN-induced signaling.

- Ezekowitz, Massachusetts General Hospital, Boston: Lifethreatening hemangiomas.
- A.W. Yasko, M.D. Anderson Cancer Center, Houston, Texas: Giant cell tumors of bone.



A. Eggermont, J. Folkman



J. Darnell, B. Williams

Meeting of the Editorial Advisory Panel: Digital Image Archive on the American Eugenics Movement

September 30–October 1

FUNDED BY National Human Genome Research Institute, National Institutes of Health

ARRANGED BY D. Micklos, Dolan DNA Learning Center, Cold Spring Harbor Laboratory J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory

SESSION 1: Welcome and Review

Overview of Image Archive Full-text Searching Bulletin Board New Collections: Ellis Island, CSHL, Estabrook Archives Banbury Center Meeting

SESSION 2: Discussion of NIH Restrictions and Conditions for Lifting "People under Scrutiny," Potential for Abuse, and Concern about Re-exploration of Disabled People

Conditions fulfilled:

Additional EAP member Posting of editorial policy Use agreement

Conditions remaining:

EAP discussion of separating site into educational and archival components Report of previous Working Group discussion Site use and relevant site feedback Resolution SESSION 3: Tour of Dolan DNA Learning Center

SESSION 4: Independent Exploration of Eugenics Site, Bioinformatics Lab Assignment of new images to topic areas

SESSION 5: Discussion of Future Plans Collection trip to Eugenics Society and University College Archives, London Future collection trips



S. Selden, P. Lombardo, and P. Ryan at the Dolan DNA Learning Center.

Making Vaccines for the Developing World: Access to and Deployment of New Technologies

October 9–11

FUNDED BY Albert B. Sabin Vaccine Institute, Inc.

ARRANGED BY M. Moree, PATH/Malaria Vaccine Initiative, Seattle, Washington P.K. Russell, Albert B. Sabin Vaccine Institute, Potomac, Maryland

Co-Chairpersons:

L.K. Gordon, VaxGen, Inc., Brisbane, California R. Rabinovich, PATH/Malaria Vaccine Initiative, Rockville, Maryland

Welcome and Introductions:

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

- D.L. Douglas, Albert B. Sabin Vaccine Institute, New Canaan, Connecticut
- P.K. Russell, Albert B. Sabin Vaccine Institute, Potomac, Maryland
- R. Rabinovich, PATH/Malaria Vaccine Initiative, Rockville, Maryland and
- Lance K. Gordon, VaxGen, Inc., Brisbane, California: Charge to the conference.
- **P.K. Russell,** Albert B. Sabin Vaccine Institute, Potomac, Maryland: Recommendations from previous meetings.
- R.T. Mahoney, International Vaccine Institute, Sedona, Arizona: Management of intellectual property.
- **H. Kettler,** Institute for Global Health, San Francisco, California: Development of intellectual property: The Biotechnology Foundation.
- SESSION 1: Case Studies: Access to Technologies for the Developing World

Chairperson: M. Moree, PATH/Malaria Vaccine Initiative, Seattle, Washington

- R. Insel, University of Rochester Medical Center, New York: Pneumococcal vaccines.
- M.A. Liu, Bill & Melinda Gates Foundation, Seattle, Washington: DNA vaccine technology.

SESSION 2: Perspectives

Chairperson: P.K. Russell, Albert B. Sabin Vaccine Institute, Potomac, Maryland

T. A. Young, Texas A&M University System, College Station: Academic technology transfer office—Rewards, motivations, accountability.

L. Gordon, VaxGen Inc., Brisbane, California: Biotech—Strategies for the development and partnering of platform technologies.

R. Rabinovich, PATH/Malaria Vaccine Initiative, Rockville, Maryland: NGOs—Access to platform technologies.

SESSION 3: Small Group Sessions: Identification of Problems

How to access and compile scientific data for the evaluation of

- platform technologies for products for the developing world? Can the initial licensing step be used to gain access to platform
- technologies for the developing world?
- How can licensing practices for companies be modified to further access?
- What different access to technology strategies may be necessary for products that have dual markets vs. products that only have a developing world market?

SESSION 4

- Reporting from Small Group Discussions: Chairperson: R. Rabinovich, PATH/Malaria Vaccine Initiative, Rockville, Maryland
- Recommendations for Action: Chairperson: L.K. Gordon, VaxGen, Inc., Brisbane, California
- Future Agenda: Chairperson: P.K. Russell, Albert B. Sabin Vaccine Institute, Potomac, Maryland



C. Schirvel, R. Insel

Cortical Maps

October 13-16

FUNDED BY Marie H. Robertson Memorial Fund for Neurobiology

ARRANGED BY D. Chklovskii, Cold Spring Harbor Laboratory A. Koulakov, University of Utah, Salt Lake City

Welcome and Introduction:

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

SESSION 1

Chairperson: A. Koulakov, University of Utah, Salt Lake City

- N. Swindale, University of British Columbia, Vancouver: Visual cortex polymaps.
- G.G. Blasdel, Harvard University, Boston, Massachusetts: Optical imaging in primate visual cortex.
- A. Grinvald, The Weizmann Institute of Science, Rehovot, Israel: Visualization of cortical architecture and dynamics.
- A. Koulakov, University of Utah, Salt Lake City: Wiring econo-

SESSION 2

Chairperson: D. Chklovskii, Cold Spring Harbor Laboratory

- Z.F. Kisvarday, Ruhr-University Bochum, Germany: Area- and age-related changes of pinwheel center positions in relation to ocular dominance map.
- E. Kaplan, Mount Sinai School of Medicine, New York, New York: Color, size, and all the rest: How do they all fit inside the visual cortex?
- M. Sur, Massachusetts Institute of Technology, Cambridge: Orientation maps and local processing in visual cortex.

my and polymaps.

- D. Chklovskii, Cold Spring Harbor Laboratory: Orientation preference maps: A wiring optimization approach.
- D.C. Van Essen, Washington University School of Medicine, St. Louis, Missouri: Cortical maps and mappings between monkeys and humans.
- J.C. Horton, University of California, San Francisco: Lessons for column formation in primate striate cortex from a precise topographic map generated from the shadows of retinal blood vessels.
- K.D. Miller, University of California, San Francisco: Which properties should be organized into maps?—A developmental model.



G. Blasdel, S. Löwell

SESSION 3

Chairperson: A. Grinvald, The Weizmann Institute of Science, Rehovot, Israel

- S. Löwell, Leibniz Institute for Neurobiology, Magdeburg, Germany: Is there a genetic influence on the layout of visual cortical maps?
- U.T. Eysel, Ruhr-University of Bochum, Germany: Optical imaging of cortical maps and the effects of visual cortex lesions: A demonstration of general robustness and subtle modifiability of cortical maps.
- D. Fitzpatrick, Duke University, Durham, North Carolina: Relating patterns of connectivity to functional maps in the

SESSION 4

Chairperson: N. Swindale, University of British Columbia, Vancouver, Canada

- J.S. Lund, University of Utah, Salt Lake City: Anatomical substrates for local and global integration of visual information: Intrinsic and feedback connections of macaque V1 cortex.
- A. Shmuel, University of Minnesota, Minneapolis: Functional organization of the feedback connection from V2 to V1 of the primate.
- A.W. Roe, Yale University School of Medicine, New Haven, Connecticut: The ANDs, and NOTs of feature-specific inte-

SESSION 5

Chairperson: G.G. Blasdel, Harvard University, Boston, Massachusetts

- D.-S. Kim, University of Minnesota Medical School, Minneapolis: Functional MRI of cortical maps—Scopes, future, and limitations.
- V. Dragoi, Massachusetts Institute of Technology, Cambridge: Inhomogeneities in the structure of orientation maps and their consequences for cortical function.
- A. Das, The Rockefeller University, New York, New York: Corti-

visual cortex.

- E.M. Callaway, The Salk Institute for Biological Studies, La Jolla, California: Relationships between afferent input, local circuits, and functional organization of primary visual cortex.
- G.J. Goodhill, Georgetown University Medical Center, Washington, D.C.: The effect of variable elastic topologies on the structure of ocular dominance and orientation maps.
- L. Krubitzer, University of California, Davis: Cortical maps: Genetic and epigenetic contributions to the phenotype.

gration in V1 and V2 of the primate.

- K. Obermayer, Berlin, Germany: Role of nonlinear intracortical interactions in cortical map formation.
- F. Wolf, Max-Planck Institute, Gottingen, Germany: Are orientation preference maps optimized for visual function?
- M.V. Tsodyks, The Weizmann Institute of Science, Rehovot, Israel: Visual maps and population activity in the visual cortex.

cal architecture and its role in early vision.

- M. Rosa, Monash University, Victoria, Australia: Small brains, great maps: The visual cortex in a dwarf primate, the marmoset monkey.
- P. Ak, Mount Sinai School of Medicine, New York, New York: Representation of spatial frequency selectivity in the mammalian primary visual cortex.



Banbury Conference Center

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J.P. Morgan H&Q/Cold Spring Harbor Laboratory Executive Conference on Controlling Cancer

October 18-20

ARRANGED BY

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

SESSION 1

- J.D. Watson, Cold Spring Harbor Laboratory: Welcoming remarks.
- D. Hanahan, Hormone Research Institute, University of California, San Francisco: Cancer as an organ.

SESSION 2

- S. Lowe, Cold Spring Harbor Laboratory: Genes, cell death, and therapies.
- C. Sawyers, Jonsson Comprehensive Cancer Center, University of California, Los Angeles: Gleevec and other kinase inhibitors in cancer therapies.
- R. Kerbel, Sunnybrook and Women's Health Sciences Centre, Toronto, Canada: Anti-angiogenic drugs as a new therapeutic approach for cancer.



L. Hudson, J. Watson

SESSION 3

- V. Mittal, Cold Spring Harbor Laboratory: DNA array technology and cancer.
- R. Lucito, Cold Spring Harbor Laboratory: Using array technology to detect genomic mutations in cancer.

SESSION 4

- K. Alitalo, Finnish Academy of Sciences, University of Helsinki, Finland: Lymphangiogenesis: A new target for cancer treatment.
- J. Schlessinger, Signaling pathways: Targets for drug discovery.
- R. Kalluri, Beth Israel Deaconess Medical Center, Boston, Massachusetts: Regulation of angiogenesis and tumor growth by vascular basement membranes.

Discussion: Cancer therapies—What next?

Closing Remarks:

J.D. Watson, Cold Spring Harbor Laboratory



G. Milne, C. Seiden

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The History and Mechanisms of Animal and Plant Evolution

October 21-24

FUNDED BY Cold Spring Harbor Laboratory Corporate Sponsor Program

ARRANGED BY J. Doebley, University of Wisconsin, Madison C. Marshall, Harvard University, Cambridge, Massachusetts N.H. Patel, HHMI, University of Chicago, Illinois

SESSION 1: Investigating Microevolutionary Change **Chairperson: N.H. Patel,** HHMI, University of Chicago, Illinois

- F. Nijhout, Duke University, Durham, North Carolina: The microevolution of developmental mechanisms.
- A. Long, University of California, Irvine: Using linkage disequilibria to dissect complex traits.
- J. Doebley, University of Wisconsin, Madison: The evolution of plant form: Examples from maize and its relatives.

SESSION 2: Variation, Adaptation, and Speciation Chairperson: J. Doebley, University of Wisconsin, Madison

P.M. Brakefield, University of Leiden, The Netherlands: Does development constrain butterfly eyespot evolution?

D.W. Schemske, Michigan State University, East Lansing:

SESSION 3: Evolution of Genetic Pathways

Chairperson: C. Marshall, Harvard University, Cambridge, Massachusetts

- C. Queitsch, University of Chicago, Illinois: Hsp90 buffers genetic variation, environmental responses and developmental stability in *Arabidopsis thaliana*.
- A.S. Wilkins, BioEssays, Cambridge, United Kingdom: How a complex genetic pathway (might have) evolved: The case of

- D. Stern, Princeton University, New Jersey: A developmental genetic approach to understanding microevolutionary morphological variation.
- G.C. Gibson, North Carolina State University, Raleigh: Will we ever have the power to dissect quantitative traits down to the nucleotide level?

Ecological genetics of adaptation and speciation.

H.A. Orr, The University of Rochester, New York: Are mathematical theories of adaptation possible?

the Drosophila sex determination pathway.

G. O'Dell, University of Washington, Seattle: The robustness of evolved genetic networks would be astonishing were it not essential.



A. Wilkins, J. Gerhart, M. Akam

SESSION 4: Plant Evolution

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

- M.J. Donoghue, Yale University, New Haven, Connecticut: Homoplasy, heterotopy, and constraints on evolution in plants.
- J. Maloof, The Salk Institute for Biological Studies, San Diego, California: Natural variation in *Arabidopsis* light signaling.

SESSION 5: Arthropod Evolution

Chairperson: M.Q. Martindale, University of Hawaii, Honolulu

- D.E.G. Briggs, University of Bristol, United Kingdom: Morphological data from Cambrian fossils: Evidence for pattern and process?
- W. Arthur, University of Sunderland, United Kingdom: How do evolutionary differences in segment number arise? Developmental and population studies of a centipede model system.
- M. Akam, University of Cambridge, United Kingdom: Arthropod relationships: New trees and their implications for the evolution of development.
- N.H. Patel, HHMI, University of Chicago, Illinois: Evolution of arthropod segmentation and body patterning.

SESSION 6: Chordate and "Basal" Metazoan Evolution Chairperson: P.W.H. Holland, University of Reading, United Kingdom

- J.C. Gerhart, University of California, Berkeley: Hemichordates and the origin of chordates.
- B.J. Swalla, University of Washington, Seattle: The role of the innate immune system in the evolution of the chordates.

- P. Janvier, Museum National d'Histoire Naturelle, Paris, France: From jawless to jawed vertebrates: A "blackbox" of vertebrate evolution.
- M.Q. Martindale, University of Hawaii, Honolulu: Axial patterning in "radially" symmetrical metazoans.

SESSION 7: Evolutionary Changes in Gene Regulation

- Chairperson: G.C. Gibson, North Carolina State University, Raleigh
- M. Ludwig, University of Chicago, Illinois: Evolution of *cis*-regulatory elements.
- G. Wray, Duke University, Durham, North Carolina: Evolution of a gene regulatory system: The Endo16 promoter of camarodont sea urchins.

SESSION 8: The Origins of Animal Multicellularity **Chairperson: N. Shubin,** University of Chicago, Illinois

- P.W.H. Holland, University of Reading, United Kingdom: Origins of animal multicellularity.
- A. Adoutte, Centre de Genetique Moleculaire du CNRS, France: The new animal phylogeny: Implications for understanding the evolution of development.

SESSION 9: The Geological Record Chairperson: J. Gerhart, University of California, Berkeley

- C. Marshall, Harvard University, Cambridge, Massachusetts: Evolution as the filtering of development by geology.
- D. Erwin, National Museum of Natural History: Evolutionary innovation: Construction of ecospace.

SESSION 10: Discussion

Co-Moderators: J. Doebley, University of Wisconsin, Madison; C. Marshall, Harvard University, Cambridge, Massachusetts; and N.H. Patel, HHMI, University of Chicago, Illinois



Wine and Cheese Party

Stability and Reversal of the Differentiated State

October 28-31

FUNDED BY	Yamanouchi USA Foundation
ARRANGED BY	 R. Lovell-Badge, National Institute for Medical Research, London, United Kingdom D. Stocum, Indiana University-Purdue University, Indianapolis J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory

Introduction and Welcome:

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

SESSION 1: Pluripotency, ES Cells, and Germ Cells

Chairperson: R. Lovell-Badge, National Institute for Medical Research, London, United Kingdom

- A. Smith, University of Edinburgh, United Kingdom: Pluripotency and lineage restriction in embryonic stem cells.
- M.A. Surani, University of Cambridge, United Kingdom: The mammalian germ line: Origin, pluripotency, and epigenetic reprogramming.

SESSION 2: Nuclear Reprogramming

Chairperson: M.C. Raff, University College, London, United Kingdom

- R. Jaenisch, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts: Nuclear cloning and the reprogramming of the genome.
- P. Mombaerts, The Rockefeller University, New York, New York: Derivation of ES cell lines via nuclear transfer in mouse.
- B. Knowles, The Jackson Laboratory, Bar Harbor, Maine: Molecular control of the oocyte to embryo transition.

- P.J. Donovan, Thomas Jefferson University, Philadelphia, Pennsylvania: Transformation of germ cells into pluripotent stem cells.
- R.G. Martinho, New York University Medical School, New York: Transcriptional regulation in *Drosophila* primordial germ cells.
- K.E. Latham, Temple University School of Medicine, Philadelphia, Pennsylvania: Incomplete or progressive reprogramming of somatic cell nuclei during cloning in mice.
- K.J. McLaughlin, University of Pennsylvania, Kennett Square: Visualizing reprogramming of Oct4 in mouse clones.



B. Carlson, D. Stocum, J. Watson

SESSION 3: Current Status of Stem Cell Regulations

Chairperson: R. Jaenisch, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts

- L. Skirboll, Office of Science Policy, NIH, Bethesda, Maryland: The development of U.S. stem cell policy.
- A. Colman, PPL Therapeutics plc, Edinburgh, United Kingdom: Patent and regulatory issues concerning research and thera-

SESSION 4: Regeneration and Reversal of the Differentiated State **Chairperson: P. Mombaerts,** The Rockefeller University, New York, New York

- D. Stocum, Indiana University-Purdue University, Indianapolis: Regenerative biology and medicine.
- J. Brockes, University College London, United Kingdom: Plasticity of the differentiated state during urodele amphibian regeneration.
- W.-S. Kim, Sogang University, Seoul, Korea: Dedifferentiation

SESSION 5: Cell Fate Decisions and Potential

Chairperson: D. Stocum, Indiana University-Purdue University, Indianapolis

- S. Huang, Children's Hospital/Harvard Medical School, Boston, Massachusetts: Switching between cell fates: Attractors in cell regulatory networks.
- D. Jackson, Cold Spring Harbor Laboratory: Control of communication and proliferation in plant stem cells.
- J.C. Watson, Indiana University-Purdue University, Indianapolis: Photoregulated protein kinases in plants.
- M. Timmermans, Cold Spring Harbor Laboratory: Suppression

SESSION 6: Adult Stem Cells and Their Potential Chairperson: A. Smith, University of Edinburgh, United Kingdom

- Diana Clarke, Curis Inc., Cambridge, Massachusetts: Understanding stem cells derived from the adult brain and pancreas.
- F.M. Watt, Imperial Cancer Research Fund, London, United Kingdom: Stem cell renewal and lineage commitment in mammalian epidermis.
- F.D. Miller, McGill University, Montreal, Canada: Isolation and characterization of multipotent adult stem cells from mammalian dermis.
- D. Meletis, Karolinska Institute, Stockholm, Sweden: Stem cells and regulation of differentiation.

SESSION 7: General Discussion

Co-Chairpersons: R. Lovell-Badge, National Institute for Medical Research, London, United Kingdom and D. Stocum, Indiana University-Purdue University, Indianapolis peutic applications of human ES cells.

J. Burley, Queen's College, Oxford, United Kingdom: Ethical and policy issues.

in the regenerating salamander limbs.

- B.M. Carlson, University of Michigan, Ann Arbor: Stability and instability of differentiation in long-term denervated and aging mammalian skeletal muscle.
- M.C. Raff, University College London, United Kingdom: Reversing direction in the oligodendrocyte lineage.

of stem cell fate during lateral organ development in maize.

- B. Petersen, University of Florida, Gainesville: In vitro trans-differentiation of adult hepatic stem cells and their potential plasticity.
- R. Lovell-Badge, National Institute for Medical Research, London, United Kingdom: Stem cell genes and cell fate decisions.



B. Knowles

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New Concepts for Clinical Cancer Trials

November 4-7

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

ARRANGED BY D. Hanahan, University of California, San Francisco J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory

Steering Committee:

J. Folkman, Children's Hospital, Boston, Massachusetts R.S. Kerbel, Sunnybrook & Women's Health Sciences Centre, Toronto, Canada J.M. Pluda, CTEP National Cancer Institute, Rockville, Maryland

Introduction and Welcome:

D. Hanahan, University of California, San Francisco J.A. Witkowski, Banbury Center, Cold Spring Harbor Laboratory

SESSION 1: Metronomic Dosing of Chemotherapy Chairperson: J. Folkman, Children's Hospital, Boston, Massachusetts

- J. Folkman, Children's Hospital, Boston, Massachusetts: The concept of metronomic dosing and its realization in traditional mouse models.
- J. Folkman, Children's Hospital, Boston, Massachusetts: Metronomic chemotherapy: The impact of suppressing p53 in tumor endothelium.

Experience(s) in the Clinic with Metronomic Chemotherapy

- E. Bergsland, University of California, San Francisco: Challenges related to putting metronomic chemotherapy into clinical practice.
- SESSION 2: Combining Metronomic Chemotherapy with Investigational Drugs Chairperson: R.S. Kerbel, Sunnybrook & Women's Health Sciences Centre, Toronto, Ontario, Canada
- R.S. Kerbel, Sunnybrook & Women's Health Sciences Centre, Toronto, Ontario, Canada: Demonstrating the principle of combining metronomic chemotherapy with investigational anti-angiogenic drugs.

Other Preclinical Results

- R. Giavazzi, Mario Negri Institute for Pharmacological Research, Bergamo, Italy: Combination treatments with experimental drugs and chemotherapies in preclinical models.
- G. Bergers, University of California, San Francisco: Assessment of metronomic chemotherapy in mouse models of multistage carcinogenesis.
- H.M. Pinedo, Free University Hospital, Amsterdam, The Netherlands: Phenomena to be considered in clinical trials aiming to achieve angiogenesis inhibition.
- S.G. Eckhardt, University of Colorado Cancer Center, Denver: Ex vivo analyses of biological activity.
- J.M. Pluda, CTEP National Cancer Institute, Rockville, Maryland: NCI experiences with new clinical trial designs and agents.

General Discussion: Issues, problems, possibilities



E. Bergsland, R. Kerbel

- Y. Takahashi, Kanazawa University, Japan: Survival without tumor shrinkage: Tumor dormancy therapy.
- B.A. Kamen, Cancer Institute of New Jersey, New Brunswick:
- chusetts: Optimal dosing entails balanced metronomic suppression of the vascular and tumor cell compartments.
- General Discussion: Issues, problems, possible actions to expedite clinical evaluation of metronomic strategies, assessing schedules and doses, biomarkers, etc.
- Pediatric experience: Empiric validation of "metronomics." L. Hlatky, Dana-Farber Cancer Institute, Boston, Massa-

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SESSION 3: Combining Metronomic Dosing of Chemotherapies with Approved Agents Being Used Offline (e.g., Celebrex and Thalidomide)

Chairperson: R.S. Kerbel, Sunnybrook & Women's Health Sciences Centre, Toronto, Ontario, Canada

R.S. Kerbel, Sunnybrook & Women's Health Sciences Centre, Toronto, Canada: Preclinical and clinical studies on metronomic antiangiogenic therapy.

Results in Animal Models or Clinical Trials/Experiences

- S. Baruchel, Hospital for Sick Children, Toronto, Canada: Lowdose chemotherapy and Celebrex as an anti-angiogenic approach: Results of a pediatric clinical trial.
- R. Buckstein, Sunnybrook Regional Cancer Centre, Toronto,

SESSION 4: The Case of Interferon- α

Chairperson: J. Folkman, Children's Hospital, Boston, Massachusetts

- J. Folkman, Children's Hospital, Boston, Massachusetts: The childhood hemangioma experience.
- R. Kalluri, Beth Israel Deaconess Medical Center, Boston, Massachusetts: Endogenous interferon suppresses angiogenesis in response to the collagen IV fragment tumstatin, an angiogenesis inhibitor.

SESSION 5: Targeting Different Stages in Cancer Progression **Chairperson: D. Hanahan,** University of California, San Francisco

D. Hanahan, University of California, San Francisco: The lessons from mouse models of multistage carcinogenesis: Stage-specific efficacy of MMP inhibitors, and tyrosine kinase receptor inhibitors.

Relevant Experiences from Clinical Trials and Mouse Models (e.g., the problems and promise of MMP-1 in Phase III Trials)

- G. Bergers, University of California, San Francisco: Targeting peri-endothelial support cells.
- J.S. Humphrey, Bristol-Myers Squibb PRI, Wallingford, Connecticut: Clinical trials of MMP1, then and now.

SESSION 6: Finale: The Path Forward

Chairperson: J.M. Pluda, CTEP National Cancer Institute, Rockville, Maryland

- J.M. Pluda, CTEP National Cancer Institute, Rockville, Maryland: The NCI perspective.
- I.M. Chico, U.S. Food and Drug Administration, Rockville, Maryland: The FDA perspective.
- A. Barge, AstraZeneca Pharmaceuticals, Cheshire, United Kingdom: Big pharma perspective.
- L. Norton, Memorial Sloan-Kettering Cancer Center, New York, New York: Oncologist perspective.

Wrap-up Discussion: Action items, initiatives, cooperative opportunities (Possible topics: How can mouse models con-

Canada: High-dose Celebrex and low-dose cyclophosphamide in relapsed/refractory Hodgkin's lymphoma. M.W. Kieran, Dana-Farber Cancer Institute, Boston, Massachusetts: Combination therapies.

- General Discussion of Topics 2 and 3: Issues, problems, opportunities. Possible actions to validate metronomic dosing strategies, and to assess when metronomic vs. MTD strategies are warranted in combinatoric trials.
- **General Discussion:** Issues, problems, possible actions to address the use of metronomic, low doses of IFNα, both alone and in combination with other agents.

- R.S. Herbst, M.D. Anderson Cancer Center, Houston, Texas: Clinical trials with RTK-1.
- L. Murray, SUGEN, Inc., South San Francisco, California: Clinical trials with RTK-1.
- J. Folkman, Children's Hospital, Boston, Massachusetts: How do you equate mouse stages to human stages, when considering the implications of stage-specific efficacy?
- **General Discussion:** Issues and problems: The path forward to address the concept of stage-specific efficacy in clinical trials.

tinue to help move forward the evaluation of these new concepts, of stage-specific efficacy, metronomic and low dosing, etc? Can/should stage-specific, metronomic, and low-dose trials be expedited for radiation and chemotherapy as single agents, so as to potentially allow broader combinatroic testing with approved and experimental drugs? If yes, how best to do so?)

A Final Question to the Participants: Should we seek to convey some of the perspectives forthcoming from this workshop to the wider community?

Epithelial and Endothelial Tube Morphogenesis

November 11–14

FUNDED BY Cold Spring Harbor Laboratory Corporate Sponsor Program

ARRANGED BY M.A. Krasnow, Stanford University School of Medicine, California W.J. Nelson, Stanford University School of Medicine, California

Welcome and Goals of Meeting:

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

SESSION 1: Mechanisms of Tube Formation—In Vitro Studies Chairperson: A.L. Hubbard, Johns Hopkins University School of Medicine, Baltimore, Maryland

K.E. Mostov, University of California, San Francisco: Epithelial tubulogenesis, polarity, and membrane traffic.

- W.J. Nelson, Stanford University School of Medicine, California: Cell dynamics in epithelial morphogenesis.
- G.E. Davis, Texas A&M University System Health Science Center, College Station, Texas: Cdc42 and Rac1 control

SESSION 2: Mechanisms of Tube Formation—In Vivo Studies **Chairperson: H. Skaer,** University of Cambridge, United Kingdom

- B.M. Weinstein, National Institute of Child Health and Human Development, Bethesda, Maryland: Studying blood vessel formation in the developing zebrafish.
- C.H. Damsky, University of California, San Francisco: Pseudovasculogenesis: Formation of a hybrid fetal/maternal vascular system during development of the human placenta.
- G.R. Dressler, University of Michigan, Ann Arbor: Cell migration

endothelial cell vacuole and lumen formation in three-dimensional extracellular matrices.

- A.L. Hubbard, Johns Hopkins University School of Medicine, Baltimore, Maryland: Vesicle traffic in polarized epithelial cells.
- M.E. Gerritsen, Genentech, Inc., South San Francisco, California: Gene expression profiling during angiogenesis in vitro.

and adhesion in the developing kidney.

- H. Skaer, University of Cambridge, United Kingdom: Cell recruitment in tubulogenesis: Parallels between *Drosophila* and mammalian kidney development.
- D.J. Andrew, Johns Hopkins University School of Medicine, Baltimore, Maryland: Genetic control of tube morphology in the *Drosophila* salivary gland.



B. Weinstein, D. Li

SESSION 3: Mechanisms of Tube Formation—Signaling and Regulation Chairperson: A.P. McMahon, Harvard University, Cambridge, Massachusetts

A.P. McMahon, Harvard University, Cambridge, Massachusetts: Tubule branching in the lung.

E. Keshet, The Hebrew University Hadassah Medical School, Jerusalem, Israel: Organ-specific induction of vascular networks in the adult.

SESSION 4: Tubulogenesis Mutants and Diseases I **Chairperson: G.J. Beitel,** Northwestern University, Evanston, Illinois

- G.J. Beitel, Northwestern University, Evanston, Illinois: Mechanisms of length and diameter control in the epithelial tubes of the *Drosophila* tracheal system.
- M. Buechner, University of Kansas, Lawrence: Regulation of the diameter of the excretory canals, a single-celled tubular epithelium in *C. elegans*.
- F. Karim, Exelixis, Inc., South San Francisco, California: Genetic dissection of pathways controlling branching mor-
- SESSION 5: Tubulogenesis Mutants and Diseases II/Engineering and Evolution of Blood Vessels
- Chairperson: D. Marchuk, Duke University Medical Center, Durham, North Carolina
- D. Marchuk, Duke University Medical Center, Durham, North Carolina: Vascular morphogenesis: What we have learned from inherited vascular dysplasias.
- D.Y. Li, University of Utah, Salt Lake City: Mouse angiogenesis mutants: Role of matrix in morphogenesis.
- D. Radisky, Lawrence Berkeley Laboratory, California: Mecha-

- W. Birchmeier, Max-Delbruck-Centrum, Berlin-Buch, Germany: c-met signaling in tubulogenesis.
- C. Samakovlis, Stockholm University, Sweden: Bnl (FGF) signaling regulates apical cell dynamics and epithelial tube length in the *Drosophila* trachea.

phogenesis and vascular remodeling.

- I. Drummond, Massachusetts General Hospital, Charlestown: Epithelial patterning and function in the zebrafish pronephric kidney.
- G. Germino, Johns Hopkins University School of Medicine, Baltimore, Maryland: Role of PKD protein in establishing and maintaining tubular structure.

nisms leading to luminal morphogenesis in the mammary gland.

M.A. Krasnow, Stanford University School of Medicine, California: Developmental control of blood cell migration by the *Drosophila* VEGF pathway: Implications for evolution of the vascular system.







