Neuroscience Symposium

Roche Innovation Center New York
September 2\textsuperscript{nd} 2014

Genes, Circuits, Behavior:
Developing New Translational Approaches for Mental Health
08:00 AM  Welcome Coffee

08:30 AM  **Luca Santarelli, Roche**  
Welcome address and Introduction to the Symposium

08:45 AM  **Juan-Carlos Lopez, Roche**  
Roche Innovation Center / Academic Relations and Collaborations

**Session 1**  Psychiatric Genetics  
**Chair:**  **Alessandro Bertolino, Roche**

09:00 AM  **Jonathan Sebat, University of California San Diego**  
Rare variants in psychiatry

09:30 AM  **Michael O‘Donovan, Cardiff**  
Common variants in psychiatry

10:00 AM  **Randy Peterson, MGH Harvard**  
Phenotypic screening and genetics in zebrafish

10:30 AM  **Pamela Sklar, Mt. Sinai**  
Discussant

10:45 AM  Coffee Break

**Session 2**  Circuits and Behaviors  
**Chair:**  **Joseph Wettstein, Roche**

11:15 AM  **Adam Kepecs, Cold Spring Harbor**  
Defining brain circuit function
Agenda

11:45 AM  Holly Moore, Columbia University  
Developmental animal models of limbic-cortical dysfunction

12:15 PM  Josh Gordon, Columbia University  
Measuring circuit dysconnectivity in rodent models from a system neuroscience approach

12:45 PM  René Hen, Columbia University  
Discussant

01:00 PM  Lunch

Session 3  Endophenotypes and Imaging
Chair: Scott Schobel, Roche

02:00 PM  Scott Small, Columbia University  
Cross-Species MR Imaging of neuropsychiatric disorders

02:30 PM  Andreas Papassotiropoulos, University of Basel  
Genome-guided drug discovery in neuropsychiatry

03:00 PM  Phil McGuire, King’s College London  
Multimodal MR Imaging of psychotic disorders

03:30 PM  Raquel Gur, University of Pennsylvania  
Discussant

03:45 PM  Coffee Break

04:15 PM  Plenary Talk: Tom Insel, National Institute of Mental Health  
From Psychiatry to Clinical Neuroscience: Challenges and Opportunities

05:15 PM  Anirvan Ghosh, Roche  
Closing Remarks
Speakers

Joshua A. Gordon, Columbia University, NY

Dr. Gordon is a psychiatrist and neuroscientist who studies the effects of genes that predispose to psychiatric illness on brain function and behavior in animal models. Dr. Gordon received his M.D. and Ph.D. degrees from the University of California, San Francisco, prior to completing a residency in psychiatry at Columbia University and the New York State Psychiatric Institute in 2001. He then completed a Research Fellowship at Columbia from 2001-2004 working with Dr. René Hen, supported by two consecutive NARSAD Young Investigator Awards.

He has taught and conducted research at Columbia University’s Department of Psychiatry since 2004 where he is now Associate Professor of Psychiatry, and Associate Director for Neuroscience Education for Columbia’s Psychiatric Residency Training Program. He has received several honors for his research, including the NARSAD Young Investigator awards, a Rising Star Award from the International Mental Health Research Organization, an APA-GlaxoSmithKline Young Faculty award, and the A.E. Bennett Research Award from the Society of Biological Psychiatry. He has also been awarded multiple grants from the National Institute of Mental Health. He is the author of over 30 publications in prestigious medical journals, including Nature, Science, Nature Neuroscience, Neuron, and the Journal of Neuroscience.

Raquel Gur, University of Pennsylvania, PA

Dr. Gur is Professor of Psychiatry Neurology and Radiology at the University of Pennsylvania Perelman School of Medicine where she directs the Neuropsychiatry Section and the Schizophrenia Research Center and is Vice Chair of Research and Development in the Department of Psychiatry. Her combined training in Psychology, Neurology and Psychiatry has provided the tools to pursue an academic career working with basic and clinical neuroscientists to advance the understanding of schizophrenia.

In directing these research endeavors, she has interacted with scientists of diverse backgrounds, conducted collaborative interdisciplinary research, mentored junior faculty and trainees, and has come to know many patients and their families. She is a member and has served in organizations including the Institute of Medicine of the National Academy of Sciences, the NIMH Council and the American Psychiatric Association task forces including the DSM-5 Psychosis work group. She is Past President of the Society of Biological Psychiatry and President Elect of the American College of Neuropsychopharmacology. NIMH has supported her research efforts and she has over 350 publications in peer-reviewed journals.
René Hen was born in Strasbourg, France, and received his Ph.D. from University Louis Pasteur under the mentorship of Pierre Chambon. After a postdoctoral stay in Richard Axel's laboratory at Columbia University, he became an assistant professor in Strasbourg. He then returned to Columbia University, where he is presently a professor of pharmacology and neuroscience and the director of the division of integrative neuroscience in the department of psychiatry.

His laboratory is using animal models to elucidate the neural substrates that underlie mood and anxiety disorders. René Hen has studied the contribution of serotonin (5-HT) receptors to pathological states such as depression and anxiety. Pharmacological studies and molecular cloning have identified several subtypes of receptors with distinct properties, signaling systems, and tissue distributions. However, the study of the function of individual serotonin receptor subtypes has been hampered by the lack of specific drugs. In addition, a number of the serotonergic drugs that are active in the treatment of neuropsychiatric disorders influence the whole serotonergic system. For example, antidepressants such as fluoxetine are 5-HT uptake blockers and potentiate the action of 5-HT at multiple post-synaptic sites. To dissect the contributions of individual serotonin receptors to physiology and behavior, mouse mutants lacking individual receptor subtypes were created in his laboratory, providing genetic models for a number of human behavioral traits such as impulsiveness, depression, and anxiety. Tissue specific and conditional knockouts have been used to identify the neural circuits underlying these traits.

Recently Hen’s lab has been investigating the function of the ventral hippocampus and the contribution of hippocampal neurogenesis to mood and cognition. Specifically, they have shown that antidepressants stimulate the division of neuronal progenitor cells in the dentate gyrus, which in turn results in an increase in the number of young neurons in the adult hippocampus. Furthermore, they have shown that hippocampal neurogenesis is required for some of the behavioral effects of antidepressants and for pattern separation. Novel therapies aimed at targeting directly hippocampal stem cells are currently under investigation for the treatment of mood disorders and age-related memory impairments.
Thomas R. Insel, National Institute of Mental Health, MD

Thomas R. Insel is Director of the National Institute of mental Health (NIMH), the component of the National Institutes of Health (NIH) committed to research on mental disorders. Dr. Insel has served as Director of this $1.5B agency since 2002. During his tenure, Dr. Insel has focused on the genetics and neurobiology of mental disorders as well as transforming approaches to diagnosis and treatment.

Prior to serving as NIHM Director, Dr. Insel was Professor of Psychiatry at Emory University where he was founding Director of the Center for Behavioral Neuroscience and Director of the Yerkes Regional Primate Center in Atlanta. Dr. Insel’s research has examined the neural basis of complex social behaviors, including maternal care and attachment. A member of the Institute of Medicine, he has received numerous national and international awards and served in several leadership roles at NIH.

Adam Kepecs, Cold Spring Harbor, NY

Adam Kepecs is an Associate Professor of Neuroscience at Cold Spring Harbor Laboratory. He studies the neural circuit mechanisms of cognition and decision making in rodents. In his research he employs quantitative behavioral paradigms, and state-of-the-art electrophysiological, optical and molecular techniques to uncover the neural processes underlying behavior.

His recent work has focused on dissecting the neural basis of decision confidence and mapping the behavioral functions of genetically identified cortical interneuron cell types. Dr. Kepecs received his bachelor’s degree in computer science and mathematics at Eötvös Loránd University, Budapest, Hungary in 1997. He then switched to studying the brain, completing his Ph.D. in the laboratory of Dr. John Lisman at Brandeis University in theoretical neuroscience. In 2002 he joined the group of Dr. Zachary Mainen at Cold Spring Harbor Laboratory where he began studying decision-making in rats. Since 2007 he has been leading an independent group at Cold Spring Harbor Laboratory.
Philip McGuire is Head of the Department of Psychosis Studies at the Institute of Psychiatry, London, and the Academic Director and joint Leader of the Psychosis Clinical Academic Group, King’s Health Partners. He is also Director of OASIS, and of the Voices Clinic. He is a Fellow of the Academy of Medical Sciences, the Royal College of Psychiatrists, the European Psychiatric Association, and the International College of Neuropsychopharmacology, and Associate Editor of the British Journal of Psychiatry.

He studied physiology and medicine at the University of Edinburgh, then worked as a research fellow in neuroscience at Yale University. After training in psychiatry at the Maudsley hospital, he was a Wellcome Research Fellow at the MRC Cyclotron Unit, Hammersmith Hospital, then a Senior Lecturer, Reader and Professor at the Institute of Psychiatry in London. He leads a clinical academic research group that is focused on determining the neurocognitive basis of psychosis and using this information to improve clinical care.
Holly Moore grew up on and around farms in the Midwest, where she developed a love for nature and a kinship with animals. Later, through a variety of jobs during her high school and college years, and through experiences in her community, she developed a strong interest in human behavior. As an undergraduate at Wright State University in Ohio, and with the guidance of a psychology professor, Holly was convinced to combine her interest in chemistry and psychology and pursue a career in neuroscience. She started on this path as a research assistant working in a laboratory, studying brain changes mediating separation responses in infant guinea pigs. Then she continued as a graduate student in neurochemistry and animal learning at The Ohio State University, then as a postdoctoral scientist studying neurophysiology and models of psychiatric disease at the University of Pittsburgh.

Through these experiences and in caring for people with mental illnesses, one of the things Holly has noticed most is the need of all creatures to feel safe, and how the feelings of safety and self-determination are attacked in mental illness. Along with mentorship, this compelled Holly to apply her interest and training in the natural sciences to the goal of understanding mental illness and lessening its burden. With that goal, Holly seeks a multi-level understanding of mental illness by studying brain structure and function from different perspectives. Her early scientific mentors include Michael Hennessy, Ph.D. (developmental psychobiology and psychoneuroimmunology), Martin Sarter, Ph.D. (psychopharmacology and animal learning), John Bruno, Ph.D. (developmental neuropharmacology), Anthony A. Grace, Ph.D. (neurophysiology and disease models in psychiatric illness), and Susan Sesack, Ph.D. (neuroanatomy).

One's education never ends in this line of work. Holly feels fortunate to have worked with incredible scientists and psychiatrists at Columbia University and the New York State Psychiatric Institute. Her recent efforts have included a translational approach to understanding a role for glutamate and inhibitory interneuron networks in hippocampal dysfunction in schizophrenia, and CNTRICS, a consortium on developing translational platforms for assessing cognition in schizophrenia and animals models.
Michael O’Donovan, Cardiff University, UK

Michael O’Donovan did his undergraduate degree in Medicine at Glasgow University, graduating in 1983. He specialized in psychiatry, with general training first at Dykebar Hospital in Paisley, and then a higher training as a Lecturer at what is now Cardiff University. He began his research career in 1989 as an MRC Training Fellow, studying gene mechanisms for benzodiazepine tolerance, and at the same time obtained a PhD in Molecular Pharmacology. From 1992-1993, he was an MRC Travelling Fellow at MIT, Cambridge, MA, USA. He was then appointed Senior Lecturer in the Department of Psychological Medicine in Cardiff where he now is Professor of Psychiatric Genetics and Deputy Director of the MRC Centre for Neuropsychiatric Genetics and Genomics. Michael O’Donovan has a broad interest in the molecular genetics and neurobiology of mental disorders and he is currently the Chair of the Schizophrenia Group of the Psychiatric Genomics Consortium, comprising of over 300 researchers from 35 countries. He is also an Honorary Consultant Psychiatrist at Cardiff and the Vale University Health Board.

Andreas Papassotiropoulos, University of Basel, CH

Andreas Papassotiropoulos is board certified psychiatrist and psychotherapist and, since 2007, full Professor of Molecular Neurosciences at the University of Basel, Switzerland. Other stations of his career led him to the University Hospital in Bonn, Germany, the University of Zürich, Switzerland, as well as research visits to the USA, amongst others at the National Institute on Aging, Bethesda, and the Translational Genomics Research Institute (TGen) in Phoenix.

His areas of expertise include the investigation of the molecular basis of human cognition and the development of improved therapies for neuropsychiatric disorders. His research combines targeted and genome-wide genetic, epigenetic and transcriptomic analyses with functional brain imaging in healthy and diseased human populations. He also studies the regulation of memory-related genes in animal models under different experimental conditions and at the level of defined neuronal subpopulations. His team uses advanced computational and mathematical approaches to generate testable hypotheses, identify the underlying genetic pathways and networks and define fundamental patterns of gene interactions. He is recipient of numerous honors and awards, amongst others the Robert-Bing-Prize, The Weizmann Lecture and, most recently, the Cloetta Prize.
Randall Peterson, Harvard University, MA

Randall T. Peterson is a chemical biologist whose research utilizes high-throughput screening technologies to discover new drug candidates for cardiovascular and nervous system disorders. Unlike conventional drug discovery programs that screen for drug candidates using simplified, in vitro assays, Dr. Peterson’s laboratory screens for drugs using living zebrafish. This approach ensures that the drug candidates discovered are active in the relevant physiological context. Several of the compounds discovered by the laboratory have become widely used research tools or preclinical drug candidates.

Dr. Peterson received his PhD from Harvard University where he studied as a Howard Hughes Medical Institute predoctoral fellow in the laboratory of Stuart Schreiber. As a graduate student, he pioneered the first in vivo high-throughput chemical screens using zebrafish. Following graduation, he completed a postdoctoral fellowship with Mark Fishman at Massachusetts General Hospital. Dr. Peterson is currently Associate Professor of Medicine at Harvard Medical School, Scientific Director of the MGH Cardiovascular Research Center-CNY, and Senior Associate Member of the Broad Institute. He is the recipient of a EUREKA award from the National Institutes of Health and is the Charles and Ann Sanders MGH Research Scholar.
Speakers

Jonathan Sebat, UC San Diego

Jonathan Sebat is Chief of the Beyster Center for Genomics of Neuropsychiatric Diseases and Assistant Professor in the Departments of Psychiatry and Cellular Molecular Medicine at UCSD. Work in his lab focuses on the identification and characterization of genetic risk factors for mental illness. His research has been central in understanding copy number variation (CNV) in the human genome and its impact on human genetic diversity and disease.

Using new genomic technologies, Dr. Sebat has pioneered the CNV-based approach to the study of common neuropsychiatric diseases, including autism and schizophrenia. These seminal studies have served to elucidate the role of rare spontaneous and inherited structural variants in neuropsychiatric disorders. His group has identified mutations at multiple sites in the genome that implicate specific neurobiological pathways in schizophrenia. Dr. Sebat is formerly an Associate Professor of Human Genetics at Cold Spring Harbor Laboratory (CSHL), an adjunct professor of biology at Stony Brook University, and a member of the Stanley Center for Psychiatric Genomics at CSHL. He received his undergraduate degree in 1995 from UC Santa Barbara; his Ph.D. in 2002 from University of Idaho. A recipient of several awards and honors, Jonathan also serves as a member of multiple working groups focused on the analysis of structural variation in humans, including the 1000 genomes project and the Psychiatric GWAS Consortium.

Pamela Sklar, The Mount Sinai Hospital, NY

Pamela Sklar is a neuroscientist, human geneticist and clinical psychiatrist investigating the genetic causes of psychiatric disorders, including schizophrenia and bipolar disorder.

A major focus of her prior work has been to identify susceptibility genes for psychiatric diseases by applying tools developed for understanding and characterizing human sequence variation. Currently, she is Chief of the Division of Psychiatric Genomics, and Professor of Psychiatry, Neuroscience, Genetics and Genomic Sciences.
Scott Small, Columbia University, NY

After graduating from NYU with a B.A. in experimental psychology, Dr. Small began the MD/PhD program at Columbia University in Eric Kandel's laboratory. Discovering that he enjoyed patient care more than he anticipated, he decided to focus exclusively on his medical training. After completing a medical internship at UCLA, a neurology residency and chief residency at Columbia, and a fellowship with Richard Mayeux, Dr. Small „returned“ to research. Informed by his prior experience studying the psychology of memory, the physiology of neurons, and the neurology of the disease he began a research program at Columbia dedicated to investigating intractable disorders of the brain. Taking a decidedly top-down approach, he pioneered the development of brain imaging tools designed to pinpoint brain dysfunction in human patients and mouse models of disease. More recently, Dr. Small has combined brain imaging with gene-expression technologies to uncover novel molecular defects underlying Alzheimer's disease and aging.

Dr. Small is the recipient of numerous awards, including the Beeson Scholar Award in Aging Research from the American Federation on Aging, the McKnight Neuroscience of Brain Disorders Award, the Derek Denny-Brown Young Neurological Scholar Award from the American Neurological Association, and the Lamport Award for Excellence in Clinical Science Research from Columbia University.
## Attendees

### Cardiff University, UK
- Michael O'Donovan

### Cold Spring Harbor, NY
- Adam Kepecs • Pavel Osten

### Columbia University, NY
- Michael Billet • Maura Boldrini • Alex Dranovsky • Annissa Abi-Dargham • Joashua A. Gordon • Jay Gingrich • René Hen • Guillermo Horga • Christophe Kellendonk • Chandana Kondapalli • E. David Leonardo • Emily Rhodes Lowry • Sander Markx • Holly Moore • Franck Polleux • Stephen Rayport • Scott Small • Ezra Susser • Hynek Wichertle

### Harvard University, MA
- Randall Peterson

### King’s College, UK
- Philip McGuire

### The Mount Sinai School of Medicine, NY
- Joel Dudley • John Fullard • Pamela Sklar • Panagiotis Roussos

### National Institute of Mental Health, MD
- Tom Insel
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<tr>
<th>Attendee</th>
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<tbody>
<tr>
<td>Katja Brose</td>
<td>Neuron, San Francisco, CA</td>
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<td>Kalyani Narasimhan</td>
<td>Nature Neuroscience</td>
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<td>Eva Chmielnicki</td>
<td>Nature Medicine</td>
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<td>Esther Blessing • György Buzsaki • Xavier Castellanos • Zhe Chen • Gordon Fishell • Donald Goff • Michael Halassa • Brendon Watson • Lucas Sjulson</td>
<td>New York University Langone Medical Center</td>
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<td>Veronika Solt</td>
<td>Private Practice, NY</td>
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<td>Winrich Freiwald • Paul Greengard • Jean-Pierre Roussarie • Eric F. Schmidt • Marc Tessier-Lavigne</td>
<td>The Rockefeller University, NY</td>
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<td>Jessica Wright</td>
<td>Simons Foundation, NY</td>
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<td>Howard Sirotkin</td>
<td>Stony Brook University, NY</td>
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# Attendees

## University of Basel, CH
- Andreas Papassotiropoulos

## University of California San Diego
- Jonathan Sebat

## University of Pennsylvania, PA
- Raquel Gur

## Roche Innovation Center, NY
- Dennis Deptula • Judith Dunn • Bruce Harris • Juan Carlos Lopez • Lisa Marcopoulos • Peter Paciorek • Jorge Quiroz • Eriene Wasef

## Roche Innovation Center Basel, CH
- Daniela Alberati • Alessandro Bertolino • Theresa Ballard • Thomas Blaettler • Céline Bouquet • Enrico Domenici • Paulo Fontoura • Anirvan Ghosh • Christophe Grund schober • George Garibaldi • Benjamin Hall • Maria C. Hernandez • Marius Hoener • Omar Khawja • Frédéric Knoflach • Annette Koerner • Lothar Lindemann • Deheeraj Malhotra • Jean-Luc Moreau • Richard Porter • Eric Prinssen • Fabrio Sambataro • Luca Santarelli • Hervé Schaffhauser • Scott Schobel • Will Spooren • Nicola Thompson • Daniel Umbricht • Joe Wettstein
Info

**Hotel**
Novotel
Times Square
226 West 52nd Street
10019 New York

Transfer to the Roche Innovation Center leaving at 07:30 AM. Please assemble 5 minutes prior at the Hotel Lobby.

**Event Location**
Alexandria Center of Life Sciences
450 East 29th Street
2nd Floor
10016 New York

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**Special Thanks to**
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MyLan Jaensch, Caroline Hügi Mazzotti: Roche Innovation Center CH