



# CONTRIBUTIONS OF POST-MORTEM TISSUE TO THE STUDY OF DEVELOPMENTAL DISORDERS

20th Anniversary of the NICHD Brain and Tissue Bank for Developmental Disorders

July 16–17, 2012

Neuroscience Center Building • 6001 Executive Boulevard • Rockville, MD 20852

## SPEAKERS



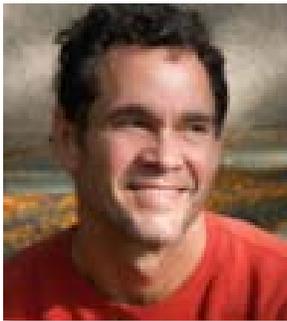
**Schahram Akbarian, M.D., Ph.D.**, is the chief of the Division of Psychiatric Epigenomics in the Department of Psychiatry and a professor in the Departments of Psychiatry and Neurobiology at Mount Sinai School of Medicine. Previously he was the director of the Brudnick Neuropsychiatric Research Institute at the University of Massachusetts Medical School and assistant, associate, and professor of psychiatry at the University of Massachusetts Medical School. His research focus is on epigenetic regulation in the nervous system, including exploration of genome organization and function across the lifespan of the normal and diseased human brain. He received his M.D. and Ph.D. in primate neuroanatomy from Freie Universitaet in Berlin, Germany, and was trained in psychiatry at Massachusetts General Hospital in Boston. He did postdoctoral work at the University of California at Irvine with the late Edward G. Jones and at the Whitehead Institute with Rudolf Jaenisch.



**Gene J. Blatt, Ph.D.**, is a professor of anatomy and neurobiology at Boston University School of Medicine. His research focused on olivocerebellar connectivity in spontaneous mutants, cortical physiology in nonhuman primates, and the limbic system (hippocampus, parahippocampal gyrus, and cingulate cortex) in nonhuman primates. He is now applying his experience and knowledge in these areas to postmortem tissue research on autism. His research findings have already had great impact in the field especially in the understanding of the pervasiveness of neurochemical defects in the autism brain, especially in the GABAergic system and its impact on circuitry and function. His current grants investigate how the glutamatergic and GABAergic systems impact the excitatory:inhibitory balance in autism and the underlying mechanisms and affected pathway(s). He also is focused in uncovering the etiologies of autism, identifying biomarkers and subgroups, and identifying common pathway(s) that are impacted in the disorder. He received his M.S. in biology from Bloomsburg University and his Ph.D. in anatomy from Thomas Jefferson University.



**Philip J. Brooks, Ph.D.**, is currently a program director in the Office of Rare Diseases Research (ORDR), as part of a detail from the National Institute on Alcohol Abuse and Alcoholism (NIAAA). Within the ORDR, now part of the NIH National Center for Advancing Translational Sciences, his main area of focus is on advancing gene therapy, other gene-based therapeutics, and genomic medicine. He also is involved in the administration and oversight of the ORDR Rare Diseases Clinical Research Network. At the NIAAA, he is a program officer in the Division of Metabolism and Health Effects, focusing on alcohol metabolism, the microbiome, and neuroinflammation. Previously he was a senior staff fellow and investigator in the Laboratory of Neurogenetics at NIAAA, where his research focused on the relationship between DNA damage and human disease, including the pathophysiology of rare genetic DNA repair disorders (xeroderma pigmentosum and Cockayne syndrome). He received his Ph.D. in neurobiology from the University of North Carolina at Chapel Hill and completed a postdoctoral fellowship at the Rockefeller University in New York.



**Eric Courchesne, Ph.D.**, is the overall director and principal investigator of the University of California San Diego (UCSD) Autism Center of Excellence, the director of the UCSD Autism Center's MRI Project on early brain development in autism, and a professor in the UCSD Department of Neurosciences. His research and the Center are dedicated to uncovering the brain bases and genetic causes of autism. He is one of the world's leading experts on the neurobiology of autism. Current magnetic resonance imaging (MRI) studies of autism aim to identify the brain structures that are abnormal at infancy in autism and to discover patterns of abnormal early brain growth. His studies of frontal cortex microstructure seek to identify abnormal developmental changes in microstructure and gene expression from early childhood to adulthood in autism. Dr. Courchesne's work has significantly contributed to scientists' understanding of the biological bases of autism and has been the source of new insights on the functional role of the frontal lobes and cerebellum.



**Florian Eichler, M.D.**, is an assistant professor of neurology at Massachusetts General Hospital (MGH) and Harvard Medical School and the director of the Leukodystrophy Clinic at MGH. Dr. Eichler runs a laboratory at MGH that explores the relationship of mutant genes to specific biochemical defects and their contribution to neurodegeneration. He recently identified two neurotoxic desoxysphingoid bases that accumulate in mutant transgenic mice and humans with HSAN1. For this work he received the Wolfe Neuropathy Research Prize from the American Neurological Association. Dr. Eichler is the principal investigator of several NIH-funded studies on neurogenetic disorders and serves on the boards of scientific advisors for the United Leukodystrophy Foundation and the National Tay Sachs and Allied Disease Foundation. He received his M.D. from the University of Vienna Medical School and was a neurogenetics research fellow at Johns Hopkins.



**S. Hossein Fatemi, M.D., Ph.D.**, is the associate chair for neuroscience and translational research for the Department of Psychiatry, a professor of psychiatry, and adjunct professor of neuroscience and pharmacology at the University of Minnesota Medical School. He is currently the principal investigator for a grant from the National Institute of Child Health and Human Development that explores biochemical mechanisms responsible for abnormal brain development in early childhood, as seen in autism; a grant from the National Institute on Drug Abuse that examines the safety and efficacy of varenicline for smoking cessation in patients with schizophrenia; and a grant from the National Institute of Mental Health that explores the role of GABAergic and Reelin signaling in schizophrenia. Dr. Fatemi's research interests include molecular causes and studies of the biological basis of schizophrenia and autism. He received his B.S. in biology from Baylor University; his M.S. and Ph.D. in anatomy from the University of Nebraska Medical Center; and his M.D. from Case Western Reserve University.



**Michio Hirano, M.D.**, is a professor at Columbia University Medical Center and a principal investigator at the North American Mitochondrial Disease Consortium. For more than two decades, he has been conducting translational neurogenetic research with a focus on neuromuscular and mitochondrial disorders. His laboratory has identified causative genes for more than 10 inherited diseases including mitochondrial neurogastrointestinal encephalomyopathy (MNGIE), LAMP-2 deficiency (Danon disease), disorders due to mitochondrial DNA (mtDNA mutations), Navajo neurohepatopathy, coenzyme Q10 deficiencies, and X-linked dominant scapulothoracic myopathy. To understand how some of these mutant genes cause diseases, Dr. Hirano's laboratory has been studying cultured cells and mouse models. He received his M.D. from the Albert Einstein College of Medicine and performed his internship at the affiliated Bronx Municipal Medical Center. He performed his neurology residency at Columbia-Presbyterian Medical Center and a neuromuscular research fellowship at Columbia-Presbyterian's H. Houston Merritt Clinical Research Center.



**Allan Jones, Ph.D.**, joined the Allen Institute to help start up the organization. Bringing extensive expertise in project leadership and high-throughput genomics operations from prior management positions at Merck and Co., Rosetta Inpharmatics, and Avitech Diagnostics, Dr. Jones was instrumental in recruiting an integrated interdisciplinary team, building the Institute's scientific operations from the ground up, and successfully driving the Allen Mouse Brain Atlas to completion. Working closely with the founders, scientific advisors, and business advisors, Dr. Jones provided strategic leadership and vision through the expansion of the Institute's portfolio of large-scale, high-impact initiatives from the mouse brain atlas through to work on the human brain. Following a focused business model for project planning and execution, he has driven multiple projects from conception to delivery as free, public resources, gaining support from the National Institutes of Health as well as various foundations and other funders to further

expand the Institute's offerings. Dr. Jones has broad scientific experience in genetics, molecular biology, and development. He received his B.S. in biology from Duke University and his Ph.D. in genetics and developmental biology from Washington University School of Medicine.



**Joel E. Kleinman, M.D., Ph.D.**, is the section chief of the Section on Neuropathology and the deputy chief of the Clinical Brain Disorders Branch of the National Institute of Mental Health. The research program of the Section on Neuropathology is primarily interested in the neuropathology of schizophrenia and seeks to determine the molecular, cellular, and genetic mechanisms that underlie this syndrome. The section investigates these mechanisms by focusing on neural circuits that are believed to underlie schizophrenia, including the prefrontal cortex, medial temporal lobe, brainstem, and striatum with special influence on molecules involved in synapse formation, plasticity, and neurodevelopment. The section also investigates susceptibility genes for schizophrenia and their relationships to these neural circuits. Dr. Kleinman's more recent work has focused on susceptibility genes for schizophrenia including COMT, GRM3, DISC1, DTNBP1, GAD1, KCNH2, and NRG1. In particular, his group has been interested in studying allelic variations in these genes and their effects on mRNA expression of specific alternate transcripts and their proteins in brain development and schizophrenia. He received his B.S., M.D., and Ph.D. from the University of Chicago. He completed an internship at San Francisco General Hospital and residencies in psychiatry and neurology at Massachusetts Mental Health Center and George Washington University Medical School, respectively.



**Janine LaSalle, Ph.D.**, is a professor of microbiology and immunology at the University of California, Davis, with memberships in the Genome Center, Rowe Program in Human Genetics, and the M.I.N.D. Institute. She is the chair of the Genetics Graduate Group at UC Davis, is on the editorial board of the journals *Human Molecular Genetics* and *Molecular Autism*, and is on the scientific advisory boards of the International Rett Syndrome Foundation and the Dup15q Alliance. The research focus in Dr. LaSalle's laboratory is on epigenetics of neurodevelopmental disorders, including autism and Rett, Prader-Willi, Angelman, and Dup15q syndromes. Dr. LaSalle's laboratory uses genomic and epigenomic technologies to investigate the role of DNA methylation and MeCP2 in the pathogenesis of Rett syndrome and autism spectrum disorders. Dr. LaSalle's laboratory has more recently been taking integrative genetic and epigenomic approaches to investigate the role of persistent organic pollutants such as flame retardant PBDEs and long-lived PCBs in mouse models and human postmortem brain samples. She received her Ph.D. in immunology from Harvard University.



**Roger Little** is a Senior Advisor at the National Institute of Mental Health. As senior advisor he keeps NIMH leadership informed about topics related to science, science policy, and trans-NIH initiatives. He also often takes on special projects, one of these is the NIH Human Neurobiobank. This is a coalition of 3 NIH institutes (NIMH, NICHD, and NINDS) working to improve the process of Brain and Tissue banking to make more human tissues available for research. His regular responsibilities include serving as a Liaison for NIMH to the NIH Common Fund, Neuroscience Blueprint, and for Public Private Partnerships. In this role he works closely with NIMH Program Staff and with Program Staff from other NIH institutes to coordinate NIMH involvement in these various activities. His areas of focus since coming to the NIMH have been psychiatric and molecular genetics. From 1998-2004 he was a post-doc at the CDC-NIOSH where he conducted basic molecular neurobiology research focused on the neural signaling pathways that mediate the brain's response to injury. Dr. Little has been recognized with over 16 awards since he began at the NIMH in 2004. Dr. Little's academic background includes Bachelor's degrees in Biology and English from the University of Vermont (1987), a Master of Science degree in Neurotoxicology (1995), and a Ph.D. in Molecular Neurobiology (1998) both from New York University. His doctoral work involved cloning and characterizing a novel G-coupled protein receptor (the calcium-independent receptor of alpha-Latrotoxin or CIRL) involved in synaptic signaling which was identified because it is a specific receptor for one of the toxins in black widow spider venom. His Masters work involved the signaling mechanisms involved in the activation of astroglial cells following brain injury.



**Jonathan Pevsner, Ph.D.**, is an associate professor in the Department of Neurology at the Kennedy Krieger Institute and in the Department of Psychiatry and Behavioral Sciences at the Johns Hopkins University School of Medicine. Dr. Pevsner's laboratory studies the molecular basis of childhood neurological disorders, including autism, Down syndrome, and other chromosomal disorders. His lab has developed a series of software tools for the analysis of genetic relatedness using single nucleotide polymorphism (SNP) data. He is the recipient of multiple teaching awards, including the Johns Hopkins University School of Medicine's Professor's Award for Distinction in the Basic Sciences and Teacher of the Year. He received his bachelor's degree in psychology from Haverford College and his Ph.D. in pharmacology and molecular sciences from the Johns Hopkins School of Medicine, where he identified an odorant-binding protein. He then conducted postdoctoral research at the Stanford University School of Medicine, where he specialized in synaptic transmission.



**Nenad Sestan, M.D., Ph.D.**, is a professor of neurobiology at Yale University School of Medicine. His research interest is molecular evolution and development of neuronal circuits of the human cerebral cortex. Research in his laboratory investigates how neurons acquire distinct identities and form precise connections in the developing cerebral cortex, a part of the brain involved in a variety of higher cognitive, emotional, sensory, and motor functions. They also study how these developmental processes have changed during evolution and in human disorders. The first primary reason to study these problems is to explore what it is about our brain that makes us human. The most important distinction between humans and other species is largely thought to reside in the unique features of human brain development, especially the way in which intricate neuronal circuits of the cerebral cortex are wired. The second is to understand why humans suffer from certain brain diseases. The emergence of intricate neuronal circuits has given us remarkable cognitive abilities but may also have increased our susceptibility to disorders such as autism and schizophrenia. An important element of his research is the integration of complementary approaches at the interface of developmental neurobiology, molecular biology, comparative genomics, and genetics. To achieve this, we combine analyses of evolutionarily conserved developmental mechanisms using the genetically tractable mouse model, comparative analyses to identify human-specific features of brain development, and genetic and molecular analyses of disorders of human cognitive development. He received his M.D. from the University of Zagreb and his Ph.D. from Yale University School of Medicine.



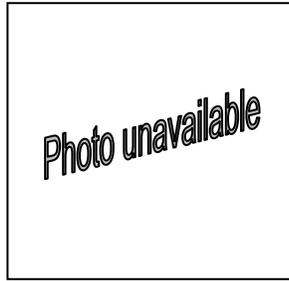
**Audrey Thurm, Ph.D.**, is a licensed child clinical psychologist. She is a staff scientist in the Pediatrics and Developmental Neuroscience Branch. Currently, she serves as an investigator of the ongoing study "Clinical and Immunological Investigations of Subtypes of Autism," aimed at finding meaningful subtypes of the disorder. In addition, she supervises the screening protocol for the branch. Dr. Thurm has worked at the National Institute of Mental Health (NIMH) since 2002, serving in the extramural division as chief of both the Autism and Social Behavior Program and the Compulsive and Repetitive Behaviors Program until moving to the Intramural Program. She was a recipient of the NIH Director's Group Award for scientific and programmatic contributions to research on autism and an NIMH Group Award for contributions to intramural research on autism. She received her undergraduate degree in human development from Cornell University and her Ph.D. in child clinical psychology from DePaul University. She completed her internship at Boston Children's Hospital/Harvard Medical School and a postdoctoral fellowship at Johns Hopkins School of Medicine.



**Bryan Traynor, M.B., M.D., Ph.D., M.M.Sc., M.R.C.P.I.**, is the chief of the Neuromuscular Diseases Research Unit in the Laboratory of Neurogenetics at the National Institute on Aging and an adjunct assistant professor at Johns Hopkins University. Previously he was a staff neurologist at Massachusetts General Hospital and an instructor in the Harvard Medical School. Dr. Traynor is best known for his work aimed at understanding the genetic etiology of amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease. He led the international consortium that identified a pathogenic hexanucleotide repeat expansion in the C9ORF72 gene as the underlying mutation in a large proportion of familial ALS and frontotemporal dementia as well as the more common, sporadic forms of both neurodegenerative diseases. He is a member of the scientific review committee of The ALS Association, a member of the Integration Panel for the Congressionally Mandated Department of Defense ALS Research Program, and has sat on various NIH Study Sections. He received his medical degree and his medical doctorate in the epidemiology and genetics of ALS from University College Dublin Medical School. He completed an internal medicine residency in Dublin, followed by a neurology residency and a neuromuscular fellowship at Massachusetts General Hospital and Brigham and Women's Hospital, Boston. He received his masters in medical science on drug discovery and clinical trial design from Harvard University and Massachusetts Institute of Technology and his Ph.D. on the genetics of ALS from his alma mater.



**Christopher A. Walsh, M.D., Ph.D.**, is Bullard Professor of Pediatrics and Neurology at Harvard Medical School, the chief of the Division of Genetics at Boston Children's Hospital, an investigator at the Howard Hughes Medical Institute, and an associate member of the Broad Institute. Previously he was the director of the Harvard-MIT combined M.D.-Ph.D. training program and the chief of genetics at Children's Hospital. Dr. Walsh's research has focused on the development, evolution, and function of the cerebral cortex, the part of our brain responsible for our highest cognitive abilities. He has pioneered the analysis of human genetic diseases that disrupt the cerebral cortex, including autism, intellectual disability, seizures, and cerebral palsy, identifying genetic causes for more than a dozen brain diseases of children. His research entails worldwide collaborations with physicians and families. He received his M.D. and Ph.D. from the University of Chicago. After completing a neurology residency and chief residency at Massachusetts General Hospital, he completed a fellowship in genetics at Harvard Medical School.



**Jerzy Wegiel, V.M.D., Ph.D.**, is the head of the Morphometry Laboratory at the New York State Institute for Basic Research in Developmental Disabilities. The concept unifying the research program of the Morphometry Laboratory is integration of clinical, neuropathological, morphometric, immunocytochemical, and biochemical methods to identify the mechanisms leading to abnormal brain development, maturation, and aging in individuals with autism and Down syndrome. Studies of developmental changes, mechanisms, and neurodegeneration are the foundation for understanding the causes of developmental disorders, developing prevention strategies, and developing new treatment strategies. This work may result in improvement of diagnosis, prevention, and treatment of autism and Down syndrome. Current projects include the Autism Brain Atlas; detection of neuropathological, immunocytochemical, and biochemical markers of abnormal brain development in autism; identification of the mechanisms leading to early onset of amyloidosis, neurofibrillary degeneration, and accelerated neuronal loss in Down syndrome; and characterization of the role of minibrain kinase (Mnb/Dyrk1A) in abnormal brain development and degeneration in Down syndrome.



**H. Ronald. Zielke, Ph.D.**, is the director of the National Institute of Child Health and Human Development Brain and Tissue Bank for Developmental Disorders and a professor of pediatrics and chief of the Division of Brain Research at the University of Maryland, Baltimore. Previously he was the principal investigator of a program project, "The Metabolic and Developmental Aspects of Mental Retardation." The research focused on energy metabolism in the brain. Additional studies addressed transport of large branch chain amino acids and regulation of the enzymes glutamine synthetase and glutaminase. He adopted microdialysis techniques for measuring oxidative metabolism in the living brain. Other research focused on sudden infant death syndrome. He received his Ph.D. in biochemistry from Michigan State University and completed two postdoctoral fellowships, one at Michigan State University and one in the Genetics Unit of Massachusetts General Hospital.