Workshop on Natural History Studies of Rare Diseases:
Meeting the Needs of Drug Development and Research

NIH Campus • Bethesda, MD — May 16 –17, 2012

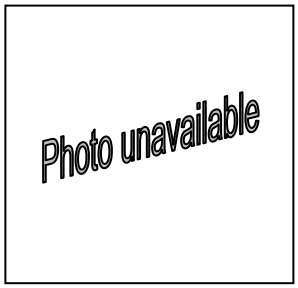
Speakers

Christopher P. Austin, M.D., is the director of pre-clinical innovation at the National Center for Advancing Translational Sciences, a new center at the National Institute of Health; its purpose is to speed the delivery of new drugs, diagnostics, and medical devices to patients. Previously, he was the senior advisor to the director for translational research at the National Human Genome Research Institute and founded the National Center for Chemical Genomics. He also worked in the private sector, focusing on genome-based discovery of novel targets and drugs. He received his M.D. from Harvard Medical School and completed his internship in medicine and his residency in neurology at Massachusetts General Hospital.

Nuria Carrillo, M.D., is the staff clinician for the Therapeutics for Rare and Neglected Diseases (TRND) program. She is a pediatrician and a geneticist with expertise in both rare and neglected diseases. She currently leads natural history studies and clinical trials for TRND projects. Prior to joining the TRND program, her research focused on clinical translational aspects of inborn errors of metabolism, biomarker development using LC-MS/MS, and gene therapy studies. She has considerable experience with natural history studies and clinical trials. She completed her pediatric residency at Georgetown University Hospital and her clinical and biochemical genetic fellowship at the NIH and Children"s National Medical Center.

Lawrence Charnas, M.D., Ph.D., is the medical director of translational medicine in the Human Genetic Therapies Division at Shire Human Genetic Therapies. He is the Shire medical lead in the joint development program with Acceleron of ACE031, a soluble ActRIIb receptor being developed for Duchenne muscular dystrophy and a pediatric study of Firazyr for hereditary angioedema. He also served as medical lead for the development project of an enzyme replacement therapy in globoid cell leukodystrophy (Krabbe disease). Prior to joining Shire, he was an associate professor of pediatrics and neurology at the University of Minnesota, working on the treatment of adrenoleukodystrophy and other lysosomal storage diseases with hematopoietic cell transplant. He developed expertise in a number of rare genetic diseases including cystinosis, osteogenesis imperfecta, and the oculocerebrorenal syndrome of Lowe. He received his B.A. in chemistry from Cornell University; his M.D. and Ph.D. in genetics from the University of Pennsylvania; and clinical training in adult neurology at Johns Hopkins Hospital, medical and biochemical genetics at the National Institute of Child Health and Human Development, and pediatric neurology at the University of Minnesota.

Karen S. Chen, Ph.D., is the chief scientific officer and chief operating officer of the Spinal Muscular Atrophy Foundation, where she is responsible for overseeing the full range of scientific and drug discovery programs and managing the operations activities. She is a senior research scientist and manager with more than 25 years of experience, including 15 years in industry, planning, directing, and conducting preclinical research. She has managed departments and groups working on a variety of projects for the discovery and development of novel therapeutics for neurological disorders. Previously Dr. Chen was the director of neurosciences and head of the Alzheimer Disease and Neurodegeneration Group at Roche Palo Alto and the director of pharmacology and head of the In Vivo Neurodegeneration and Behavior Groups at Elan Pharmaceuticals, working primarily on therapies for Alzheimer disease and Parkinson disease. She received her A.B. from Harvard University; her Ph.D. in neurosciences from the University of California, San Diego; and her postdoctoral training at Genentech, investigating neurotrophic factor therapies for neurodegenerative conditions.

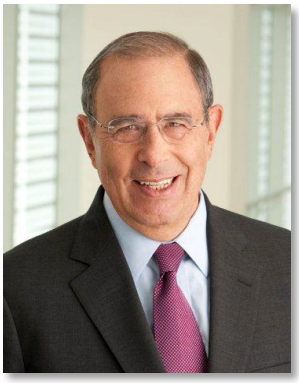


Basil T. Darras, M.D., is the associate neurologist-in-chief for clinical services, director of the Neuromuscular Program, and director of the Residency Training Program at Children's Hospital Boston. He also is a professor of neurology at Harvard University. His specialties include cerebral palsy, child neurology, electromyography, neuromuscular disorders, and spinal muscular atrophy. He received his M.D. and performed his internship at the University of Athens Medical School and performed his residency at the Nassau County Medical Center. He performed fellowships at Tufts-New England Medical Center and Yale University School of Medicine.

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.

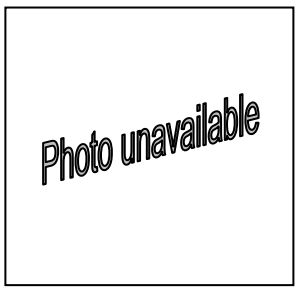
Maria L. Escolar, M.D., is the director of the Program for the Study of Neurodevelopment in Rare Disorders (NDRD). The NDRD was established at the University of North Carolina, Chapel Hill, in order to help children and their families understand the overall impact of rare neurological diseases on the child's development. She has 17 years of experience as a practicing clinician and researcher. Dr. Escolar has authored multiple original manuscripts, including two New England Journal of Medicine articles. She is nationally and internationally known for her work in neurodevelopment of children with leukodystrophies and mucopolysaccharidosis. Her research focuses on behavioral and neuroimaging outcome measurements and natural history studies. She is a graduate of the Escuela Colombiana de Medicina, received an M.S. in human nutrition from Columbia University, and completed a residency in general pediatrics and a fellowship in child development and behavior at Cornell University Medical Center. She is board certified in pediatrics and neurodevelopmental disabilities.

Patricia Furlong is the founder and president of Parent Project Muscular Dystrophy, a nonprofit organization that is dedicated to Duchenne muscular dystrophy (DMD). Her focus and determination have helped grow the organization from a small group of parents who were frustrated by the lack of investment in DMD research into one of the leading DMD authorities in the world. The mission of Parent Project Muscular Dystrophy is to improve the treatment, quality of life, and long-term outlook for all individuals affected by DMD through research, advocacy, education, and compassion. She also serves on the Muscular Dystrophy Coordinating Committee of the U.S. Department of Health and Human Services.



John I. Gallin, M.D., is the director of the NIH Clinical Center (CC). The CC serves the clinical research needs of 17 NIH institutes and is the largest hospital in the world totally dedicated to clinical research. Dr. Gallin has overseen the design and construction of a new research hospital for the CC, the Mark O. Hatfield Clinical Research Center, which opened to patients in 2005; the establishment of a new curriculum for clinical research training now offered globally; and development of new information systems for biomedical translational and clinical research. In 2011, under Dr. Gallin's leadership, the NIH CC received the Lasker-Bloomberg Public Service Award. While serving as CC director, Dr. Gallin has continued to be an active clinician and researcher. His primary research interest is in a rare hereditary immune disorder, chronic granulomatous disease (CGD). His laboratory described the genetic basis for several forms of CGD and has done pioneering research that has reduced life-threatening bacterial and fungal infections in CGD patients. Dr. Gallin received his M.D. from Cornell University Medical College. He performed his medical internship and residency at New York University's Bellevue Hospital Medical Center and received postdoctoral training in basic and clinical research in infectious diseases at NIH.

Stephen C. Groft, Pharm.D., is the director of the Office of Rare Diseases Research (ORDR) of the National Center for Advancing Translational Sciences (NCATS) at the National Institutes of Health (NIH). His major focus is on stimulating research on rare diseases and developing information about rare diseases and conditions for health care providers and the public. To help identify research opportunities and establish research priorities, the ORDR has co-sponsored more than 1,200 rare diseases-related scientific conferences with the NIH research Institutes and Centers. Current activities include establishing patient registries for rare diseases, developing an inventory of available biospecimens from existing biorepositories, developing an educational module on rare diseases for middle school children, establishing a public information center on genetic and rare diseases, developing an international rare diseases research consortium, maintaining the Rare Diseases Clinical Research Network, and providing a special emphasis clinic with senior clinical staff for patients with undiagnosed diseases at NIH's Clinical Research Center Hospital. He received his B.S. in pharmacy and his Pharm.D. from Duquesne University.



Meral Gunay-Aygun, M.D., is a pediatrician biochemical geneticist who is a staff clinician at the National Human Genome Research Institute (NHGRI) and associate professor of pediatrics at John Hopkins University School of Medicine. She also is the principal investigator of the intramural clinical trial "Clinical and Molecular Investigations into Ciliopathies" (www.clinicaltrials.gov identifier NCT00068224).The study aims to delineate clinical characteristics of individual ciliopathies, generate genotype-phenotype correlations, and identify outcome parameters for design of future treatment trials. Ciliopathy patients including autosomal recessive polycystic kidney disease and Joubert syndrome patients are evaluated for renal, hepatic, ophthalmic, neurological, metabolic, and endocrine features. To date, 250 patients are enrolled; some are followed prospectively. She received her M.D. from Hacettepe University School of Medicine in Turkey, completed a pediatric residency and genetics fellowship at Case Western Reserve University, and completed a biochemical genetics fellowship at NHGRI.

Patrick Haslett, M.D., is the medical lead for the Shire Human Genetic Therapies Sanfilippo syndrome programs in Shire's translational medicine group. Previously he consulted in the areas of inflammation and immunomodulation as a member of Department of Translational Medicine at Eli Lilly and Company and obtained training in cellular immunology and clinical investigation at the Rockefeller University. He was a faculty member at the University of Miami, Florida, where he conducted independent research into the immunopathogenesis of HIV disease and leprosy. He spent the early part of his career in general medical practice in rural Zambia, with a major emphasis on HIV/AIDS diagnosis and care, and worked with the AIDS Clinical Trials Group. He received his M.D. from St. George's Hospital Medical School of the University of London and completed a fellowship in infectious diseases at New York University.

Wendy J. Introne, M.D., is a pediatrician and clinical and biochemical geneticist participating in clinical research on rare genetic diseases at the National Institutes of Health (NIH). She has been an investigator on numerous natural history protocols on a spectrum of rare diseases, including alkaptonuria, Chediak-Higashi syndrome, Hutchinson-Gilford progeria syndrome, and Smith-Magenis syndrome. Several of these studies have laid the groundwork for consequent treatment trials. Previously, she worked in the Pediatric Genetic Division of the Department of Pediatrics at Strong Memorial Hospital in Rochester, New York. Dr. Introne completed her residency in pediatrics at Children's National Medical Center in Washington, DC, and fellowship training in clinical and biochemical genetics at the NIH.

Petra Kaufmann, M.D., M.Sc., is the director of the Office of Clinical Research (OCR) at the National Institute of Neurological Disorders and Stroke (NINDS). In this capacity, she oversees the clinical research programs funded by NINDS. The OCR fosters clinical research that increases our understanding of the cause, diagnosis, treatment, and prevention of neurological diseases and translates scientific discoveries into improved therapies for people living with neurological diseases worldwide. Prior to joining NINDS, Dr. Kaufmann was a tenured associate professor of neurology at Columbia University, where she worked clinically in the neuromuscular division, the electromyography laboratories, and the pediatric neuromuscular clinic. Her research focused on the clinical investigation of spinal muscular atrophy (SMA), amyotrophic lateral sclerosis (ALS), and mitochondrial diseases. She received her M.D. from the University of Bonn, Germany, and her M.Sc. in biostatistics from Columbia's Mailman School of Public Health. She completed an internship in medicine at St. Luke's/Roosevelt Hospital in New York City and trained in neurology and clinical neurophysiology at Columbia University. She did a postdoctoral fellowship in molecular biology of mitochondrial diseases at Columbia's H. Houston Merritt Center for Muscular Dystrophies and Related Diseases.

Edward M. Kaye, M.D., is the senior vice president and chief medical officer at AVI BioPharma. Previously he served as group vice president for clinical development and therapeutic head for lysosomal storage disorders and neurodegenerative diseases at Genzyme. He held additional leadership roles in clinical development and medical affairs at Genzyme and developed specific experience with pediatric neuromuscular conditions. He played a leadership role in gaining Myozyme's approval for Pompe disease and oversaw collaborations in this field, including the development of ataluren for Duchenne muscular dystrophy (DMD). Prior to joining Genzyme, he was chief of biochemical genetics at Children's Hospital of Philadelphia, associate professor of neurology and pediatrics at the University of Pennsylvania School of Medicine, and chief of pediatric neurology and director of the Barnett Mitochondrial Laboratory at St. Christopher's Hospital for Children in Philadelphia. He received his medical education and

pediatric training at Loyola University Stritch School of Medicine and University Hospital; received his child neurology training at Boston City Hospital, Boston University; and completed his training as a neurochemical research fellow at Bedford VA Hospital, Boston University.

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Priya S. Kishnani, M.D., is the division chief of medical genetics and the C.L. and Sue Chen Professor of pediatrics at Duke University Medical Center. Her clinical interests include glycogen storage disease with a focus on Types I, II, III, and IX; lysosomal storage diseases such as Gaucher, Pompe, and Fabry diseases; Down syndrome; and management and treatment of metabolic disorders. Her research interests include a multidisciplinary approach to the care of individuals with genetic disorders in conjunction with clinical and bench research. She received her training at Topiwala National College in Bombay, India. She performed residencies in pediatrics at Bombay University and Duke University Medical Center and a fellowship in genetics and metabolism at Duke University Medical Center.

Jeffrey P. Krischer, Ph.D., is a professor and head of the Division of Biostatistics and Informatics, director of the Pediatric Epidemiology Center in the Department of Pediatrics, and professor in the Department of Computer Science and Engineering at the University of South Florida. Previously he was professor and chief of the Division of Epidemiology and Biostatistics and adjunct professor in the Department of Statistics at the University of Florida, associate director of the H. Lee Moffitt Cancer Center and Research Institute, and professor in the Department of Interdisciplinary Oncology at the University of South Florida College of Medicine. His research interests lie in the design and conduct of clinical trials. He received his Ph.D. in applied mathematics from Harvard University.

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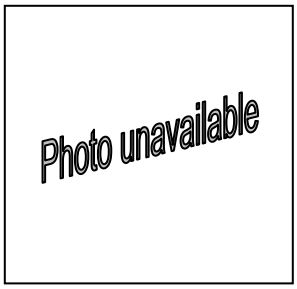
Craig M. McDonald, M.D., is a professor and chairman of the Department of Physical Medicine Rehabilitation, director of the Neuromuscular Disease Clinics, director of the National Institute on Disability and Rehabilitation Research (NIDRR) Rehabilitation Research Training Center in Neuromuscular Diseases, director of the Spina Bifida Program, and director of the neuromuscular disease clinics at the University of California Davis. He also is director of the Electrodiagnostic Laboratory at the Shriners Hospital for Children Northern California. His research interests include novel clinical endpoint development in neuromuscular diseases, clinical trials and natural history studies in muscular dystrophies, metabolic syndrome, and energy expenditure in childhood disabilities. He received his M.D. from the University of Washington School of Medicine.

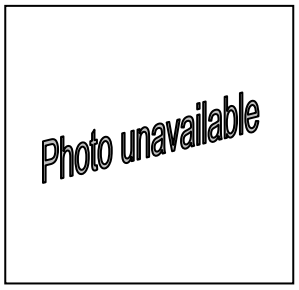
John McKew, Ph.D., is chief of the Therapeutic Development Branch of the Therapeutics for Rare and Neglected Diseases Program at the National Center for Advancing Translational Sciences (NCATS) at the National Institutes of Health (NIH). The Therapeutics for Rare Diseases program and the Bridging Interventional Development Gaps program are in this branch, which is focused on building an intramural research group tasked with soliciting and advancing projects through discovery and preclinical development. Previously, he led a chemistry group dedicated to the cardiovascular, musculoskeletal, and metabolic diseases therapeutic areas at Wyeth Research and worked in the inflammation therapeutic area resulting in multiple compounds entering clinical evaluation. He received his Ph.D. in organic chemistry from the University of California.

Richard A. Moscicki, M.D., is the head of clinical development and senior vice president at Genzyme and has a faculty appointment at Harvard Medical School. Prior to integration with Sanofi, Dr. Moscicki was the chief medical officer and senior vice president of clinical development and medical affairs with global responsibility for all aspects of clinical research, medical affairs, regulatory issues, and pharmacovigilance at Genzyme. In his role at Genzyme, he was involved in the development and approval of nine products. Prior to joining Genzyme, Dr. Moscicki served as a staff physician at Massachusetts General Hospital (MGH) and was the director of the training program in allergy and clinical immunology for several years. Dr. Moscicki received his M.D. from Northwestern University. He served his residency in internal medicine at the Medical Center Hospital of Vermont and held clinical and research fellowships in clinical immunology and immunopathology at MGH and Harvard Medical School. He is board certified in internal medicine, allergy and immunology, and diagnostic laboratory immunology.



Anne Pariser, M.D., is the associate director for rare diseases in the Office of New Drugs (OND) at the Food and Drug Administration's (FDA's) Center for Drug Evaluation and Research. She established the Rare Diseases Program in OND in 2010 and currently is working to support, facilitate, and accelerate the development of therapeutics for rare diseases. The Rare Diseases Program concentrates on the development of biomedical and regulatory science, rare disease-specific training and education, and policy and guidance generation for rare disease product review and regulation. Dr. Pariser also is actively involved in numerous collaborations within FDA and with drug developers, other governmental agencies, advocacy groups, and other stakeholders to further the development of treatments for rare diseases. Prior to founding the Rare Diseases Program, she was a medical officer and team leader in OND, where she worked almost exclusively on the review and regulation of products for rare genetic disorders.

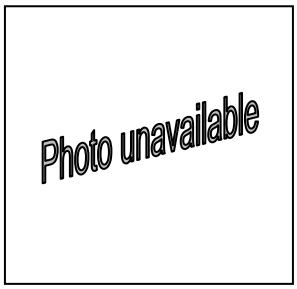
Jane S. Paulsen, Ph.D., is a professor of psychiatry, neurology, and psychology; chief of the psychology service; and director of the Huntingdon's Disease Center of Excellence at the University of Iowa. Her areas of interest include Huntington's disease, Alzheimer disease, schizophrenia, dementia, psychoses, and tardive dyskinesia. She received her M.A. from Columbia University and her Ph.D. from the University of Iowa.



David Pearce, Ph.D., is the vice president of Sanford Research. His research focuses on juvenile Batten disease, an incurable genetic disorder that causes a fatal protein malfunction in children. Previously he was an associate professor of biochemistry and biophysics and neurology in the Center for Neural Development and Disease at the University of Rochester School of Medicine and Dentistry. He received his B.S. with honors in biological sciences from Wolverhampton Polytechnic and his Ph.D. from the University of Bath. He received postdoctoral training at the University of Rochester and Oxford University.

Gayatri R. Rao, M.D., J.D., is the acting director of the Office of Orphan Products Development (OOPD) at the Food and Drug Administration (FDA), working to advance the development and evaluation of medical products that demonstrate promise for prevention, diagnosis, or treatment of rare diseases. Dr. Rao oversees the Orphan Grants Program, Orphan Drug Designation Program, Humanitarian Use Device Program, and Pediatric Device Consortia Program. Previously, she provided advice on a wide range of issues related to medical devices, combination products, clinical trials, and human subject protection at the FDA's Office of the Chief Counsel. She graduated from the University of Medicine and Dentistry of New Jersey, New Jersey Medical School and earned both her law degree and bioethics masters degree from the University of Pennsylvania, where she concentrated on healthcare and FDA-related issues. Following law school, she worked for a private law firm in Washington, DC, focusing primarily on food and drug and other health care-related matters, including matters related to orphan products.

Elsa G. Shapiro, Ph.D., is a professor of pediatrics and neurology in the Division of Pediatric Clinical Neuroscience at the University of Minnesota. She is known for research in neurobehavioral and neuroimaging manifestations of genetic neurodegenerative disorders. She developed methods of longitudinal assessment of neurocognitive functions, delineated the neurocognitive phenotypes of several genetic disorders, studied the relationship between quantitative neuroimaging and neuropsychology in treated and untreated children, and examined the characteristics of dementia in children with neurodegenerative disease. She is the co-principal investigator of the Lysosomal Disease Network and principal investigator of Longitudinal Studies of Brain Structure and Function in the Mucopolysaccharidoses. She also has a strong interest in the effects of poverty on the developing brain; she previously led a large study of the effects of lead and other social and biological variables on the cognitive development of high-risk inner city children and now consults on the effects of cerebral malaria and HIV on neurodevelopment in Ugandan children. She received her Ph.D. in clinical psychology from the University of Minnesota.

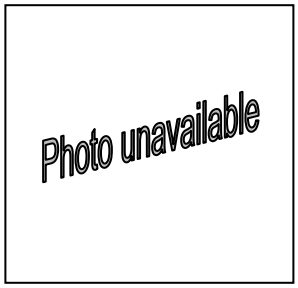


Annette Stemhagen, Dr.P.H., F.I.S.P.E., is the senior vice president of safety, epidemiology, registries, and risk management at United BioSource Corporation (UBC), where she provides strategic consultative services to pharmaceutical and biotechnology clients and assists other UBC groups in developing and implementing creative and innovative study design solutions to meet client needs. She holds adjunct faculty appointments at the University of Pennsylvania School of Medicine Center for Epidemiology and Biostatistics and the Temple University School of Pharmacy. She received her undergraduate degree from the University of Pennsylvania and her masters and doctoral degrees from the University of Pittsburgh Graduate School of Public Health in Epidemiology.

Marshall L. Summar, M.D., is the chief of the Division of Genetics and Metabolism, the Margaret O'Malley Chair of Molecular Genetics, and the director of the NIH-sponsored Clinical Research Center at Children's National Medical Center. He is an international expert in inborn errors of metabolism, particularly those in the urea cycle. His research involves translational studies taking basic molecular genetics research and developing direct clinical applications. His work has piloted treatments from the rare disease field to common conditions, especially in the intensive care and emergency room setting. His work in the urea cycle has involved the development of treatment protocols, translational research, and basic molecular research into these rare defects in nitrogen metabolism. He is one of the founding investigators of the Urea Cycle Disorders Consortium and serves on the three-member executive board. Current research projects involve clinical trials to improve the outcomes of patients with congenital heart defects, acute lung injury, asthma, and premature infants using compounds from metabolic pathways he studies. He received his M.D. from the

University of Tennessee and did postdoctoral work in genetics and pediatrics at Vanderbilt University Medical Center.

P.K. Tandon, Ph.D., is a senior vice president and clinical science officer in clinical development at Genzyme Corporation and an associate professor in the Department of Biostatistics and Epidemiology at the Boston University School of Public Health. As a member of Genzyme's senior executive leadership team, his key responsibilities span across translational medicine and early clinical development, late clinical development, and life cycle management (registries) domains. As a senior member of the research and development executive team, Dr. Tandon provides strategic direction and leadership in the clinical development of Genzyme products and in the design, analysis, and reporting of late stage clinical trials. He is responsible for the Company's biomedical data sciences and informatics support of the registries. Dr. Tandon interfaces with other senior leaders to formulate and execute clinical development strategies and resourcing and business development opportunities and leads major efforts in establishing clinical development opportunities in India. Prior to joining Genzyme, he was a senior director at Astra USA and an assistant director of clinical biostatistics at Sterling Research Group. He received his Ph.D. from The Ohio State University and holds an executive program diploma from the Sloan School of Management of MIT.



Marc K. Walton, M.D., Ph.D. is the associate director for translational medicine in the Office of Translational Sciences at the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA). His position focuses on fostering both internal and external science and policies to support innovative approaches to therapeutic development and includes biomarkers, clinical study design and analysis methods, liaison to external consortia and other agencies, and rare diseases. Previously he was a medical officer working on clinical trials of biological products for neurological disorders at the FDA's Center for Biologics Evaluation and Research (CBER). Oversight of several additional clinical areas was added upon his appointment as branch chief in the Division of Clinical Trial Design and Analysis. A subsequent move to the Office of Policy in the Office of the Commissioner gave involvement in a broad range of agency-wide issues. He received his graduate degrees from the University of Chicago. Following a neurology residency at the University of Rochester, he moved to the National Institute of Neurological Disorders and Stroke, researching neurotransmitter responses in embryonic spinal cord.