Accelerating Science—Advancing Medicine

The Department of Psychiatry at Icahn School of Medicine at Mount Sinai is at the forefront of discovery and academic productivity. In 2014, during an extraordinarily difficult time for public research funding, our National Institutes of Health (NIH) funding rose to $26 million, placing us at No. 6 among the nation’s leading academic psychiatry departments. By comparison, in 2010 our NIH funding totaled $15 million.

At the same time, Mount Sinai’s scientists made major contributions to our understanding of the genetics of schizophrenia and autism, resulting in studies that appeared in Nature and other top journals.

Pamela Sklar, MD, PhD, founding Chief of Mount Sinai’s Division of Psychiatric Genomics, led one of the largest and most comprehensive genetic studies of psychiatric illness ever done and in 2015 was elected to the Institute of Medicine of the National Academy of Sciences. The work of Dr. Sklar and her research team suggests new ways of thinking about the role of rare mutations in schizophrenia.

We are also testing novel therapeutics for patients with Phelan-McDermid Syndrome (PMS), a genetically defined subtype of autism typically caused by a defect in the SHANK3 gene. The treatments are based on discoveries that originated in Mount Sinai’s basic neuroscience and genetics laboratories, and are being directed by Alexander Kolevzon, MD, Associate Professor of Psychiatry and Pediatrics.

Through a five-year, $6 million NIH grant from the Rare Disease Clinical Research Network, Mount Sinai is collaborating with nine other medical centers and leading PMS research to provide a foundation for best clinical practices and the development of novel therapeutics for patients with the disease.

Additional highlights in this Chair’s Report include the introduction of our new Residency/PhD program and recent developments in bipolar disorder.

Using Insulin-Like Growth Factor-1 to Treat Autism

A clinical trial under way at the Icahn School of Medicine at Mount Sinai is expected to help determine whether the use of insulin-like growth factor-1 (IGF-1) can improve social and language skills in children with Phelan-McDermid Syndrome (PMS), a subtype of autism spectrum disorder (ASD).

PMS, which is also known as 22q13 Deletion Syndrome, results from a mutated or missing copy of the SHANK3 gene. IGF-1 is the first medication ever used to treat PMS in a controlled clinical trial.

The trial is being led by Alexander Kolevzon, MD, Clinical Director of the Seaver Autism Center and Associate Professor of Psychiatry and Pediatrics, with funding from the National Institute of Mental Health. Eighteen participants, who range in age from 5 to 12, will undergo two 12-week treatment periods in which they will receive either IGF-1 or a placebo.

Children with PMS typically suffer from developmental delays, intellectual disability, motor skills deficits, and delayed or absent speech.

“This clinical trial is part of a paradigm shift to develop precision medicines based on genetic findings specifically to treat the core symptoms of autism,” says Joseph Buxbaum, PhD, Director of the Seaver Autism Center at Icahn School of Medicine at Mount Sinai. “Our study will
Mount Sinai Offers a Combined Psychiatric Residency and PhD Track

The Department of Psychiatry at Icahn School of Medicine at Mount Sinai now offers students a uniquely designed MD/PhD track that integrates post-doctorate training in genetics or neuroscience with psychiatry residency training. The seven-year Psychiatry Residency + PhD Program began in the fall and is being funded by the National Institute of Mental Health (NIMH)—under the R25 mechanism.

Mount Sinai’s new program improves upon the current method of training MD/PhD candidates, which emphasizes a separation between research and clinical skills. The unintended consequence of this separation, however, often leads to a decline in the physician’s basic science skills and the need to retrain after residency. As a result, many MD/PhDs choose not to pursue research after their residency training is completed.

“Our unique program will prepare residents for a career in translational medicine by allowing them to conduct sophisticated academic work while training in clinical care,” says Ronald O. Rieder, MD, Professor of Psychiatry, Director of the Psychiatry Residency Program and Vice Chair for Education in the Department of Psychiatry at Mount Sinai. “There is an urgent need in psychiatry to conduct translational research that will help us understand the neurological systems that underlie psychiatric disorders and translate findings in basic science into clinical trials.”

Four medical students will be accepted into the program via the National Residency Matching Plan and are expected to receive financial incentives through the National Institutes of Health’s Loan Repayment Program.

Residents will also receive instruction in scientific writing and attend grant proposal writing workshops to help prepare publications, their theses, and post-residency research funding.

Cognitive Impairment in Bipolar Disorder

Researchers at Icahn School of Medicine at Mount Sinai have been awarded a grant from the National Institute of Mental Health (NIMH) to study the predictors of cognitive impairment in 350 bipolar patients. The team is being led by Katherine Burdick, PhD, Associate Professor of Psychiatry and Neuroscience and Chief of Neuropsychology Research.

In addition to testing for the severity of neurocognitive impairment, the investigators will examine the clinical and biological predictors of cognitive impairment in bipolar disorder (BPD) by incorporating sleep quality, tasks of affective processing, and markers of inflammation in the blood. Dr. Burdick is also studying cognitive predictors across the full range of psychosis in a study funded by the U.S. Department of Veterans Affairs.

In a separate NIMH study, Dr. Burdick is using the psychostimulant modafinil to treat the cognitive problems that are found in patients with BPD.

Forty-eight patients with BPD who are not experiencing acute symptoms will receive either modafinil or a placebo for a period of eight weeks. The investigators will evaluate the effects of the drug on sleep quality, daytime wakefulness, and neurocognition. Cognitive functioning will be assessed using the MATRICS Consensus Cognitive Battery supplemented by several domain-specific tasks at the beginning, middle, and end of the study.

In another NIMH-funded study, Dr. Burdick will investigate the effects of the medication pramipexole in patients with bipolar disorder. One-hundred patients will be randomly assigned to receive pramipexole, a medication that is commonly used to treat Parkinson’s disease, or a placebo for 12 weeks.

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evaluate the impact of IGF-1 when compared with placebo on autism-specific impairments in socialization and associated symptoms of language and motor disability.”

Dr. Buxbaum and Seaver Center researchers had previously discovered that deficits in nerve cell communication caused by loss of SHANK3 can be reversed after two weeks of treatment with IGF-1.

The Seaver Center also was one of five leading institutions to receive a five-year, $100 million grant from the National Institutes of Health to create clinical trials to determine whether oxytocin nasal spray improves social functioning in children with ASD. The study participants will receive oxytocin or a placebo for the first six months of the trial. Afterward, all participants will receive the oxytocin for an additional six months.

“This is the largest treatment study with oxytocin to date and will ultimately include 300 children between the ages of 5 and 17 with an ASD diagnosis,” says Dr. Kolevzon.