NIH Grant to support Mount Sinai Research Program to Create Biological Network Model of Alzheimer's Disease in partnership with New York Stem Cell Foundation

Team to apply innovative analytical methods to gain new insights and identify potential therapies

NEW YORK – September 18, 2013 /Press Release/ —

Scientists from the Icahn School of Medicine at Mount Sinai, in partnership with the New York Stem Cell Foundation (NYSCF), and other institutions, have been awarded a multi-year grant from the National Institutes of Health (NIH) to study Alzheimer's disease.

This study will apply innovative analytical methods to large-scale molecular, cellular, and clinical data from Alzheimer's patients to construct biological network models and gain new insights into the complex mechanisms of the disease, and identify potential therapeutic targets. Biological network models are complex mathematical representation of large amounts of data. These networks provide a unified map that integrates not only the key genes involved in a disease but also the biological pathways that those genes control.

The NIH grant will enable the research team at Mount Sinai and partner institutions to build upon the discovery published earlier this year in the journal *Cell* of a network of genes as a key mechanism driving Late Onset Alzheimer's Disease (LOAD) through involvement in the inflammatory response in the brain.

Eric Schadt, PhD, The Jean C. and James W. Crystal Professor of Genomics at the Icahn School of Medicine at Mount Sinai, and Director of the Icahn Institute for Genomics and Multiscale Biology, will be a principal investigator in the study. "With this grant, we can continue to build and refine our predictive model of Alzheimer's disease to yield valuable insights into the complex mechanism of the disease and potential therapies. In the same way that sophisticated predictive mathematical models drive decision making in the global financial markets, our field of medical research has begun to rely on network models to derive meaning from vast amounts of patient data, enabling better understanding and treatment of human disease," said Dr. Schadt.

The research team will use several cellular and animal models to validate the actions of individual genes, as well as entire molecular networks predicted to drive the disease. The team will also employ a computational approach to test if any existing drugs currently used for other conditions are capable of modulating the Alzheimer's networks and can, therefore, be repurposed for Alzheimer's disease treatment or prevention.

This award was among several new research grants totaling $45 million NIH announced on Wednesday to advance the National Plan to Address Alzheimer's Disease, a national effort that aims to find effective interventions for Alzheimer's by 2025. Dr. Neil Buckholtz, Director of the Division of Neuroscience at the National Institute on Aging, which leads the NIH Alzheimer's research program, noted that the array of

grants will fund innovative basic research as well as new clinical trials aimed at finding therapies to prevent the disorder. “We are delighted to support Dr. Schadt and his team in their important work of applying novel analytical methods to build models of this complex disorder,” Buckholtz said. “Additionally, this funding supports their computational approach investigating the repurposing of existing drugs as treatment for Alzheimer’s-- a key objective set forth in the Alzheimer’s Plan.”

Scott Noggle, PhD, Director of the NYSCF Laboratory and the NYSCF – Charles Evans Senior Research Fellow for Alzheimer’s Disease, is a principal investigator in the study. Dr. Noggle and his team at NYSCF will be the lead stem cell partner in this study. They will generate stem cell lines from Alzheimer’s patient samples and produce Alzheimer’s neurons that will be used as a platform for validating drug targets that are identified through computational analysis. Stem cell lines and neurons will be produced on the unique NYSCF Global Stem Cell Array™, a proprietary automated technology platform that for the first time makes it possible to create identical stem cell lines from a large number of patients in a massively parallel process. “Existing approaches have failed to identify new Alzheimer’s therapeutics and I believe that through this multifaceted approach we will collaborate to identify and validate new drug targets for Alzheimer’s patients,” said Dr. Noggle.

Sam Gandy, MD, PhD, Director of the Center for Cognitive Health at Mount Sinai, and a principal investigator in the study, said, “This research is of paramount importance. Currently, no effective disease-modifying or preventive drugs exist for common, late onset Alzheimer’s Disease. Despite decades of intensive conventional research, the causal chain of mechanisms behind sporadic Alzheimer’s Disease has remained elusive. This multi-scale, computational strategy, combined with target validation in mouse brain, in fly brain, and in stem cell models, is already providing clues to unanticipated pathways and new drug discovery opportunities. ”

The NIH grant (NIA grant AG 046170-01) was developed under a recent initiative specifically aimed at understanding the complexity of Alzheimer’s disease. This approach assumes that Alzheimer’s might best be explained and treated by focusing on genes that serve as “hubs” that interconnect a group of genes. These hubs are important because when they malfunction and cause Alzheimer’s, they cause predictable malfunctions of the entire group of connected genes. This approach leverages big data and high-end analytical approaches to develop predictive network models of disease. As a key source of data, the Mount Sinai investigators will study gene expression in brains from the Mount Sinai Alzheimer’s Disease Research Center Brain Bank that specializes in identifying the very earliest stages of Alzheimer’s. This brain bank was established over 35 years ago and is considered to be one of the best such resources in the world.

About The Mount Sinai Medical Center

The Mount Sinai Medical Center encompasses both The Mount Sinai Hospital and Icahn School of Medicine at Mount Sinai. Established in 1968, the Icahn School of Medicine is one of the leading medical schools in the United States, with more than 3,400 faculty in 32 departments and 14 research institutes. It ranks among the top 20 medical schools both in National Institutes of Health (NIH) funding and by U.S. News & World Report. The Mount Sinai Hospital, founded in 1852, is a 1,171-bed tertiary- and quaternary-care teaching facility and one of the nation’s oldest, largest and most-respected voluntary hospitals. The Mount Sinai Hospital is nationally ranked by U.S. News & World Report as one of the top 25 hospitals in 7 specialties based on reputation, safety, and other patient-care factors.
For more information, visit Mount Sinai on the web, Facebook, Twitter or YouTube.

About The New York Stem Cell Foundation

The New York Stem Cell Foundation (NYSCF) is an independent research institute founded in 2005 that accelerates cures and better treatments for patients through stem cell research. NYSCF has over 45 researchers in its New York laboratory and is an acknowledged world leader in stem cell research and in

developing pioneering stem cell technologies, including the NYSCF Global Stem Cell Array™. Additionally, NYSCF supports another 60 researchers at other leading institutions worldwide through its Innovator Programs, including the NYSCF – Druckenmiller Fellowships and the NYSCF-Robertson Investigator Awards. NYSCF focuses on translational research in a model designed to overcome the barriers that slow discovery and encourage multi-institutional collaboration.

NYSCF researchers have achieved five major discoveries in the field, including: the recent creation of patient-specific bone substitutes from skin cells; the discovery of a clinical cure to prevent transmission of maternal mitochondrial diseases in December 2012; the derivation of the first-ever patient specific embryonic stem cell line (named the #1 Medical Breakthrough of 2011 by Time magazine); the discovery of a new way to reprogram stem cells; and the creation of the first disease model from induced pluripotent stem cells (also named the #1 Medical Breakthrough by Time magazine in 2008).

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