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Stamford, CT, and New York, NY — October 25, 2018 – Scientists from the Icahn School of Medicine at Mount Sinai, Eli Lilly and Company, and Sema4 released results from a proof-of-concept study demonstrating that patient-derived cells offer a more effective approach for assessing drug response than conventional methods. These findings could pave the way for streamlined drug discovery, particularly for diseases such as schizophrenia that have seen little therapeutic innovation. The study was published this week in *Nature Communications.*

Drug discovery for neuropsychiatric disorders such as schizophrenia is limited due to a lack of useful models for screening candidate treatments. Currently, all antipsychotic drugs approved by the U.S. Food and Drug Administration target the same dopamine receptor. Unfortunately, two-thirds of patients with schizophrenia have no response or only partial response to these treatments. New therapies are necessary, but without biologically relevant screening models there has been little progress.

In this new study, scientists theorized that more meaningful results could be generated from testing drug candidates on patient-derived cells, rather than on generic cell lines. They utilized cells isolated from 12 patients with schizophrenia and 12 healthy controls, generating induced pluripotent stem cells that were guided to become neural progenitor cells, the key cell type targeted for neuropsychiatric disorders. Researchers prepared a series of assays from each individual's cells, treated them with 135 different small molecules selected for their predicted or demonstrated interaction with schizophrenia-relevant biology, and analyzed gene activity. The same drugs were tested on commonly used cancer cell lines for comparison. Results clearly showed that the patient-derived cells yielded more disease-relevant information than the generic cells. In some cases, certain drugs reversed the gene expression signatures associated with schizophrenia.

"There is tremendous value in gene expression-based drug screening using patient-derived cells because it can generate results that are more reflective of disease biology," said Kristen Brennand, Associate Professor of Neuroscience, Psychiatry, and Genetics and Genomic Sciences at Mount Sinai and senior author of the paper.

"For diseases in which high-throughput phenotypic screening is challenging, transcriptomic-based screening can be highly informative and help accelerate the drug discovery process," said Radoslav Savić, Director of Scientific Collaborations at Sema4, Associate Professor of Genetics and Genomic Sciences at Mount Sinai and corresponding author of the paper.

For this study, drug screening was performed at Mount Sinai with compounds provided by Eli Lilly. Funding for the work came from Mount Sinai and Eli Lilly.

The high-throughput gene-expression profiling was performed by Genometry, Inc. (Cambridge, MA) using their L1000™ Expression Profiling assay. "L1000 was created specifically for large-scale small-molecule screening applications like this one, and the results here are impressive," said Justin Lamb, PhD, President and CEO of Genometry.

"This study nicely illustrates the importance of using an integrative genomics approach for improving drug discovery and, ultimately, patient care," said Adam Margolin, PhD, Director of the Icahn Institute for Data Science and Genomic Technology at Mount Sinai. "The results should be immediately applicable not only to drug discovery for schizophrenia but also more broadly to a wide range of diseases for which more biologically relevant screening models are long overdue."

Paper cited: Benjamin Readhead et al. Expression-based drug screening of neural progenitor cells from individuals with schizophrenia. *Nature Communications*. DOI: 10.1038/s41467-018-06515-4

About Sema4

Sema4 is a patient-centered predictive health company founded on the idea that more information, deeper analysis, and increased engagement will improve the diagnosis, treatment, and prevention of disease. A Mount Sinai Health System venture based in Stamford, Connecticut, Sema4 is dedicated to transforming healthcare by building more dynamic models of human health and defining optimal, individualized health trajectories, starting with reproductive health and oncology. Our innovative Sema4 Health Intelligence Platform is enabling us to generate a more complete understanding of disease and wellness and to provide science-driven solutions to the most pressing medical needs. Sema4 believes that patients should be treated as partners, and that data should be shared for the benefit of all.

For more information, please visit sema4.com and connect with Sema4 on Facebook, Twitter and YouTube.

About the Mount Sinai Health System

The Mount Sinai Health System is New York City's largest integrated delivery system encompassing seven hospital campuses, a leading medical school, and a vast network of ambulatory practices throughout the greater New York region. Mount Sinai's vision is to produce the safest care, the highest quality, the highest satisfaction, the best access and the best value of any health system in the nation. The System includes approximately 6,600 primary and specialty care physicians; 10 joint-venture ambulatory surgery centers; more than 140 ambulatory practices throughout the five boroughs of New York City, Westchester, Long Island, and Florida; and 31 affiliated community health centers. The Icahn School of Medicine is one of three medical schools that have earned distinction by multiple indicators: ranked in the top 20 by U.S. News & World Report's "Best Medical Schools", aligned with a U.S. News & World Report's "Honor Roll" Hospital, No. 13 in the nation for National Institutes of Health funding, and among the top 10 most innovative research institutions as ranked by the journal Nature in its Nature Innovation Index. This reflects a special level of excellence in education, clinical practice, and research. The Mount Sinai Hospital is ranked No. 18 on U.S. News & World Report's "Honor Roll" of top U.S. hospitals; it is one of the nation's top 20 hospitals in Cardiology/Heart Surgery, Gastroenterology/GI Surgery, Geriatrics, Nephrology, and Neurology/Neurosurgery, and in the top 50 in six other specialties in the 2018-2019 "Best Hospitals" issue. Mount Sinai's Kravis Children's Hospital also is ranked nationally in five out of ten pediatric specialties by U.S. News & World Report. The New York Eye and Ear Infirmary of Mount Sinai is ranked 11th nationally for Ophthalmology and 44th for Ear, Nose, and Throat, while Mount Sinai Beth Israel, Mount Sinai St. Luke's and Mount Sinai West are ranked regionally.

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