



Sema4 and Mount Sinai Use Integrative Network Analysis to Identify Potential New Lung Cancer Therapy

April 5, 2022

STAMFORD, CT – April 5, 2022 – [Sema4](#) (NASDAQ: SMFR), an artificial intelligence (AI)-driven genomic and clinical data intelligence platform company, and researchers from the Icahn School of Medicine at Mount Sinai (Icahn Mount Sinai) in New York, NY recently published a study in *Nature Communications* using network modeling to identify novel targets for treating patients with early-stage invasive lung adenocarcinoma.

“This new paper demonstrates how the synergism of *in silico*, *in vitro*, and *in vivo* technologies can accelerate the drug discovery process,” said [Eric Schadt](#), PhD, Founder and Chief Executive Officer of Sema4 and an author on the paper. “By performing an integrative network analysis of early-stage lung adenocarcinoma, together with our partners at Icahn Mount Sinai, we were able to identify a gene expression signature capable of stratifying patients for treatment and a potential novel therapeutic for these patients.”

“The approaches to diagnosing and treating early-stage lung adenocarcinoma are evolving and are based upon advances in understanding the biology and clinical activities of these tumors,” said senior author Charles Powell, MD, MBA, Janice and Coleman Rabin Professor of Medicine and Chief of Pulmonary, Critical Care and Sleep Medicine at Icahn Mount Sinai. “Our work using novel network approaches in collaboration with Sema4 to identify signatures of invasiveness and to identify drugs that can intercept progression of these cancers should contribute to advancing the understanding and outcomes for this cancer.”

Lung adenocarcinoma is the most common lung cancer in the United States. Because of its often aggressive nature, early diagnosis is critical to improving survival. The new study disentangles the molecular mechanisms underlying tumor invasion in early-stage lung adenocarcinoma to improve patients’ diagnosis, prognosis, and treatment.

“Sema4’s advanced predictive modeling and data science expertise uniquely position us to deliver value to and accelerate discovery for collaborators in the biopharma, healthcare, and research worlds,” said [Gustavo Stolovitzky](#), PhD, Chief Science Officer at Sema4. “Through this collaboration, we again proved the value of our integrative network modeling by uncovering a novel way to stratify early-stage lung adenocarcinomas into indolent and aggressive forms and positing a potential therapeutic to help patients with the aggressive type. Dependent upon clinical validation, genomic testing for the invasiveness signature could one day be incorporated into our Sema4 Signal® portfolio of precision oncology solutions to help guide treatment decisions for patients with aggressive early-stage lung adenocarcinoma.”

In the collaborative study that builds upon the NIH-funded lung cancer research program in Dr. Powell’s laboratory, researchers from Icahn Mount Sinai collected early-stage lung adenocarcinoma tumor samples and sequenced their RNA. Sema4 then analyzed the network of gene-gene interactions based on this sequencing data, resulting in the identification of a gene expression signature that can distinguish between invasive and noninvasive tumors.

“When we annotated the gene signature, we uncovered an enrichment for genes associated with tumor invasion-related functions,” said Jun Zhu, PhD, Head of Data Sciences at Sema4 and Professor of Genetics & Genomic Sciences at Icahn Mount Sinai (Dr. Zhu was the joint senior author on the paper). “We then analyzed retrospective patient data and defined a numerical index based on gene expression in the patients, which we called the ‘invasiveness score.’ We found that this invasiveness score is strongly associated with survival in multiple independent cohorts, confirming its prognostic significance.”

Researchers at Icahn Mount Sinai showed that the invasiveness score is also strongly associated with invasiveness in cancer cell lines and validated it in a mouse model of early-stage lung adenocarcinoma. The integrative network analysis identified aurora kinases as master regulators of this invasiveness and suggested that they are good targets for treating early-stage lung adenocarcinoma. Aurora kinases have known roles in tumor growth and survival in several other cancers, but this is the first confirmation of their role in early-stage lung cancer progression. Further experiments confirmed the expression of aurora kinases in tumors and found that their disruption by inhibitors decreased invasiveness behavior *in vitro*. Similarly, the use of aurora kinase inhibitors in genetically engineered mice suppressed invasion and improved survival.

“This study, combining the research and clinical expertise from Icahn Mount Sinai with Sema4’s advanced network modeling methods, is a textbook example of how *in silico* and experimental technologies can complement one another to accelerate research,” said Dr. Powell. “We look forward to continuing this collaboration with Sema4 to investigate the therapeutic application of aurora kinase inhibitors in early-stage lung adenocarcinoma further.”

The published study is based on technology developed by Mount Sinai faculty. In addition to their roles with Sema4, Drs. Schadt and Zhu remain affiliated with Icahn Mount Sinai as part-time faculty members. Mount Sinai and Mount Sinai faculty, including Drs. Schadt and Zhu, have a financial interest in Sema4. Mount Sinai also has representation on the Sema4 Board of Directors.

About Sema4

Sema4 is a patient-centered health intelligence company dedicated to advancing healthcare through data-driven insights. Sema4 is transforming healthcare by applying AI and machine learning to multidimensional, longitudinal clinical and genomic data to build dynamic models of human health and defining optimal, individualized health trajectories. Centrellis®, our innovative 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 [Twitter](#), [LinkedIn](#), [Facebook](#) and [YouTube](#).

About the Mount Sinai Health System

The Mount Sinai Health System is New York City's largest academic medical system, encompassing eight hospitals, a leading medical school, and a vast network of ambulatory practices throughout the greater New York region. Mount Sinai advances medicine and health through unrivaled education and translational research and discovery to deliver care that is the safest, highest-quality, most accessible and equitable, and the best value of any health system in the nation. The Health System includes approximately 7,300 primary and specialty care physicians; 13 joint-venture ambulatory surgery centers; more than 415 ambulatory practices throughout the five boroughs of New York City, Westchester, Long Island, and Florida; and more than 30 affiliated community health centers. The Mount Sinai Hospital is ranked on *U.S. News & World Report's* "Honor Roll" of the top 20 U.S. hospitals and is top in the nation by specialty: No. 1 in Geriatrics and top 20 in Cardiology/Heart Surgery, Diabetes/Endocrinology, Gastroenterology/GI Surgery, Neurology/Neurosurgery, Orthopedics, Pulmonology/Lung Surgery, Rehabilitation, and Urology. New York Eye and Ear Infirmary of Mount Sinai is ranked No. 12 in Ophthalmology. Mount Sinai Kravis Children's Hospital is ranked in *U.S. News & World Report's* "Best Children's Hospitals" among the country's best in four out of 10 pediatric specialties. 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* "Honor Roll" Hospital, and No. 14 in the nation for National Institutes of Health funding. *Newsweek's* "The World's Best Smart Hospitals" ranks The Mount Sinai Hospital as No. 1 in New York and in the top five globally, and Mount Sinai Morningside in the top 20 globally.

For more information, visit <https://www.mountsinai.org> or find Mount Sinai on [Facebook](#), [Twitter](#) and [YouTube](#).

Sema4 Media contact:

Radley Moss

radley.moss@sema4.com