Scientists Construct First Predictive Model of Inflammatory Bowel Disease

September 11, 2017

Integrating multidimensional data reveals complexity of immune response network

STAMFORD, Conn. & NEW YORK, NY — September 11, 2017 — Scientists at the Icahn School of Medicine at Mount Sinai Sema4, and collaborating institutions today published results of an in-depth, multi-'omics approach to characterizing the immune component of inflammatory bowel disease (IBD). These results provide new insights into the biologic networks involved in IBD with potential to identify new targets and eventually novel interventions for the treatment of patients living with IBD. The article appeared online in *Nature Genetics*.

In the United States, some 3 million adults are diagnosed with IBD, which includes Crohn's disease and ulcerative colitis and is associated with immune and inflammation mechanisms. Previous genome-wide association studies to detect the genetic source of this condition turned up more than 200 genes, but those explain just a small fraction of IBD cases.

For this study, scientists used a wide variety of data — including DNA variation, gene expression, regulatory elements, and clinical information — gathered from three different groups of patients with various stages of IBD. This deep computational dive allowed the team to model the precise biological networks involved in the immune component, resulting in the first-ever predictive model of the disease.

"These results demonstrate how much we stand to gain by organizing massive amounts of molecular and clinical data using advanced machine learning approaches that in turn can be queried to generate novel disease insights," said Eric Schadt, Sema4 CEO, Dean for Precision Medicine at Icahn School of Medicine at Mount Sinai, and senior author on the paper. "Our predictive model serves as a repository of knowledge and understanding that facilitates learning more about the development and progression of IBD, including identifying master regulators of disease that can be explored as targets for treatment."

By working directly from patient tissue samples, the research team was able to observe the effects of genes and regulatory elements on each other and represent the entire network of immune activity. The scientists then experimentally validated the top 12 genes predicted to alter that network, providing new insights into elements that regulate IBD.

"By creating multiscale predictive models of the immune component of IBD across different stages of disease, this work helps move us towards a more comprehensive understanding of the complex molecular network of this disease," said Scott Snapper, MD, PhD, Professor of Medicine at Harvard Medical School and Chair of the National Scientific Advisory Board of the Crohn's and Colitis Foundation, who was not involved in this study but is a renowned expert in the research and treatment of IBD. "I look forward to accessing this new knowledge base as highly informative to the collective efforts of the IBD research community to identity new targets and ultimately, novel treatments of IBD."

This work represents a unique collaboration between the Icahn School of Medicine at Mount Sinai, Sema4 researchers and Janssen Research & Development, LLC immunology scientists to leverage clinical research and deep genomics data.

Paper cited: Peters L *et al.* A functional genomics predictive network model identifies regulators of inflammatory bowel disease. *Nature Genetics*, doi:10.1038/ng.3947

About Sema4
Sema4 is a health information company that is committed to providing open access to data and creating practical tools that help patients, clinicians, and researchers better diagnose, treat, and prevent disease. Sema4 is constructing a more comprehensive picture of health by combining a wealth of clinical experience that informs the answers that patients and providers are seeking, the world-class academic research that illuminates new directions, and the pioneering information science that puts all the pieces together. Sema4 is a venture of the Mount Sinai Health System, an integrated health system that is internationally recognized for its excellence in research, patient care, and education.

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

About the Icahn School of Medicine at Mount Sinai
The Icahn School of Medicine at Mount Sinai is an international leader in medical and scientific training, biomedical research, and patient care. It is the medical school for the Mount Sinai Health System, an integrated health care system which includes seven hospitals and an expanding ambulatory network serving approximately 4 million patients per year.

The School has more than 1,800 students in MD, PhD, and Master's programs and post-doctoral fellowships; more than 5,600 faculty members; over 2,000 residents and fellows; and 23 clinical and research institutes and 34 academic departments. It is

ranked among the highest in the nation in National Institutes of Health funding per principal investigator. The School was the first medical school in the country to create a progressive admissions approach for students who seek early assurance of admission through the FlexMed program.

The Graduate School of Biomedical Science trains PhD and MD/PhD students, and offers master's-level programs in areas such as genetic counseling, clinical research, biomedical sciences, and public health, and an online master's degree in health care delivery leadership. The seamless connections between our medical school, graduate school, and hospital campuses provide an extraordinary environment for translating scientific discoveries into clinical treatments.

For more information, visit http://icahn.mssm.edu or find the Icahn School of Medicine at Mount Sinai on Facebook, Twitter, YouTube, and LinkedIn.

Media Contacts

Sema4
Glenn Farrell
glenn.farrell@sema4.com

Mount Sinai Press Office
(212) 241-9200
NewsMedia@mssm.edu