

GENOMICS + MULTISCALE BIOLOGY AT MOUNT SINAI SCHOOL OF MEDICINE

A Conversation with

Eric Schadt, PhD

Director of the Institute for Genomics and Multiscale Biology, Chair of the Department of Genetics and Genomics Sciences, and the Jean C. and James W. Crystal Professor of Genomics

» You are a pioneer and visionary team builder in the field of computational biology in genomics. What promise does this specialty hold to revolutionize the practice of medicine?

Computational biology and the related field of systems biology seek to provide a holistic view of living systems by modeling high-dimensional, large-scale data at the molecular, cellular, and clinical levels simultaneously. The goal is to construct predictive models of disease that will help us better understand the biological processes that are involved in the pathophysiology of disease, drug response, and treatment. For example, such models will help physicians identify the best genes to target for therapeutic interventions, locate important genes to assess disease risk or progression, and better inform patient care by matching the right treatment to the right patient at the right time. The specialty will help provide faster, safer, and more effective health care, and ultimately reduce the overall disease burden.

» Recently, you joined The Mount Sinai Medical Center as Director of the Institute for Genomics and Multiscale Biology. What is your vision for the Institute, and how will it be at the forefront of the revolution in genetics and genomics sciences?

Mount Sinai will be a leader in genetics and genomics sciences by using high-performance computing to organize all of the data that is generated at the Medical Center (see Figure 1, below). Researchers at the Institute will then apply sophisticated mathematical algorithms to that data to develop predictive models of disease. By mastering such high volumes of information, our vision is to be able to provide researchers, clinicians, and patients with the most informed, well-rounded viewpoint from which to base their decisions about treatment and therapies.



» In the scientific community you are somewhat infamous for saying that molecular biology is flawed because it focuses on one individual gene at a time rather than looking at the thousands of genes that make up biological networks. What is the "New Biology" approach you have developed and why is it the key to understanding biological systems?

My opinion is that we take a very myopic and linear view of biology. Looking at individual genes is important, but focusing on how they fit into the larger system will lead to a better understanding of common human diseases and, ultimately, more effective diagnoses and treatments.



The New Biology focuses on many moving parts at a hierarchy of scales, from the small molecular level to the large community level. To appreciate how nonlinear biology is, think about your family. When you ask your child a question, do you always get the same response? Or do you sometimes get very unexpected, hard-to-decipher responses? Biological systems—at all levels—have complex behaviors. If we want to understand them, we need to study them on a system-wide level.

» The Institute for Genomics and Multiscale Biology is one of 14 disease-oriented and core technology-based institutes at Mount Sinai. How important is interdisciplinary collaboration to the genetics revolution?

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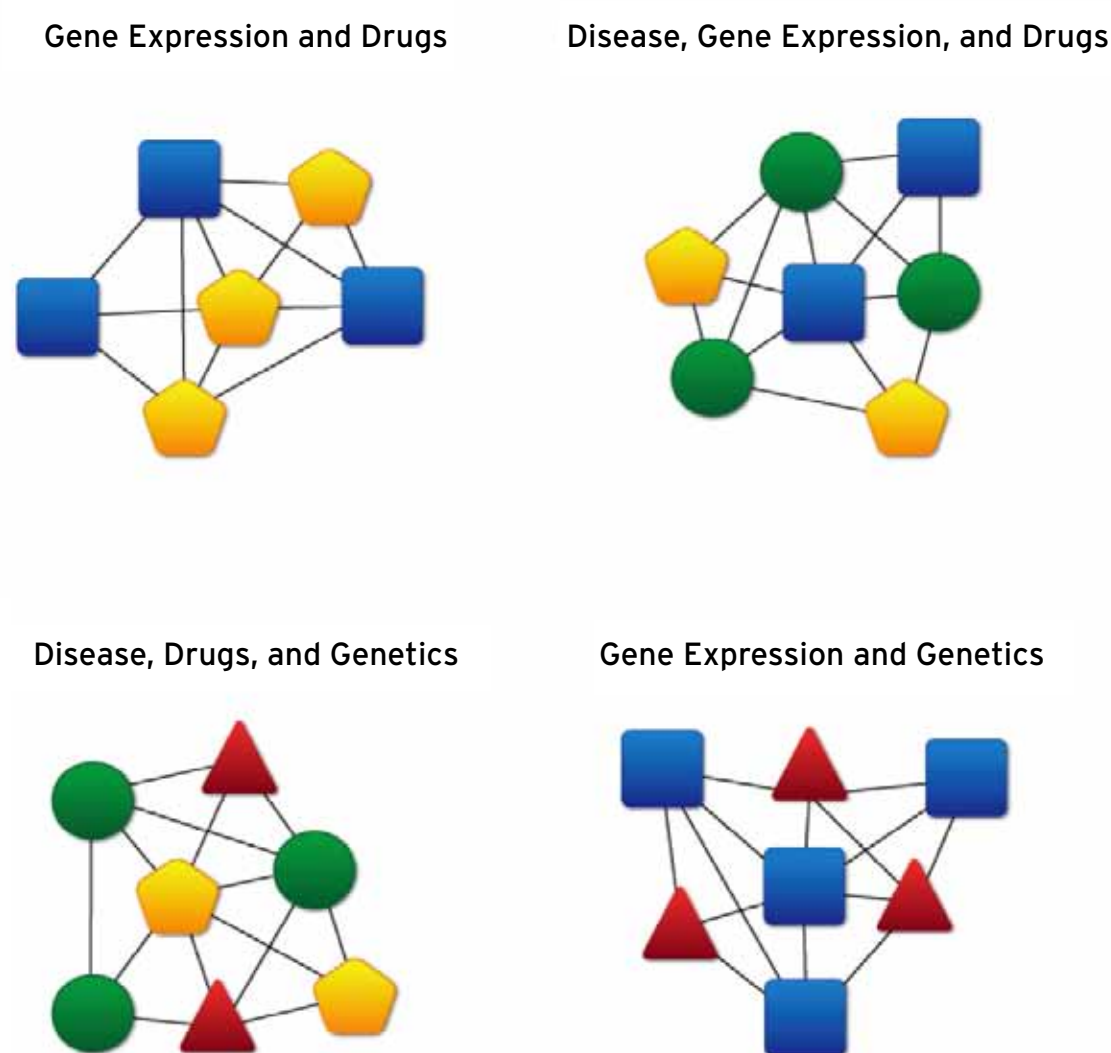


Figure 1: Networks from different data types. Drug, disease, gene expression, and genetic data generated in different combinations in coherent data sets produce reference networks that can be accessed by unique queries and inform on distinct biological relationships. The different experimental techniques used to generate the various types of networks from large, well-powered studies that involve many individuals or experimental conditions reveal different and complementary details about the network components and their contribution to emergent properties of biological systems.

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» **At the Institute, you plan to create a highly active data analytic center where researchers around the world can query and learn from the work collected at the Institute. How will other institutions and researchers help inform Mount Sinai's investigations?**

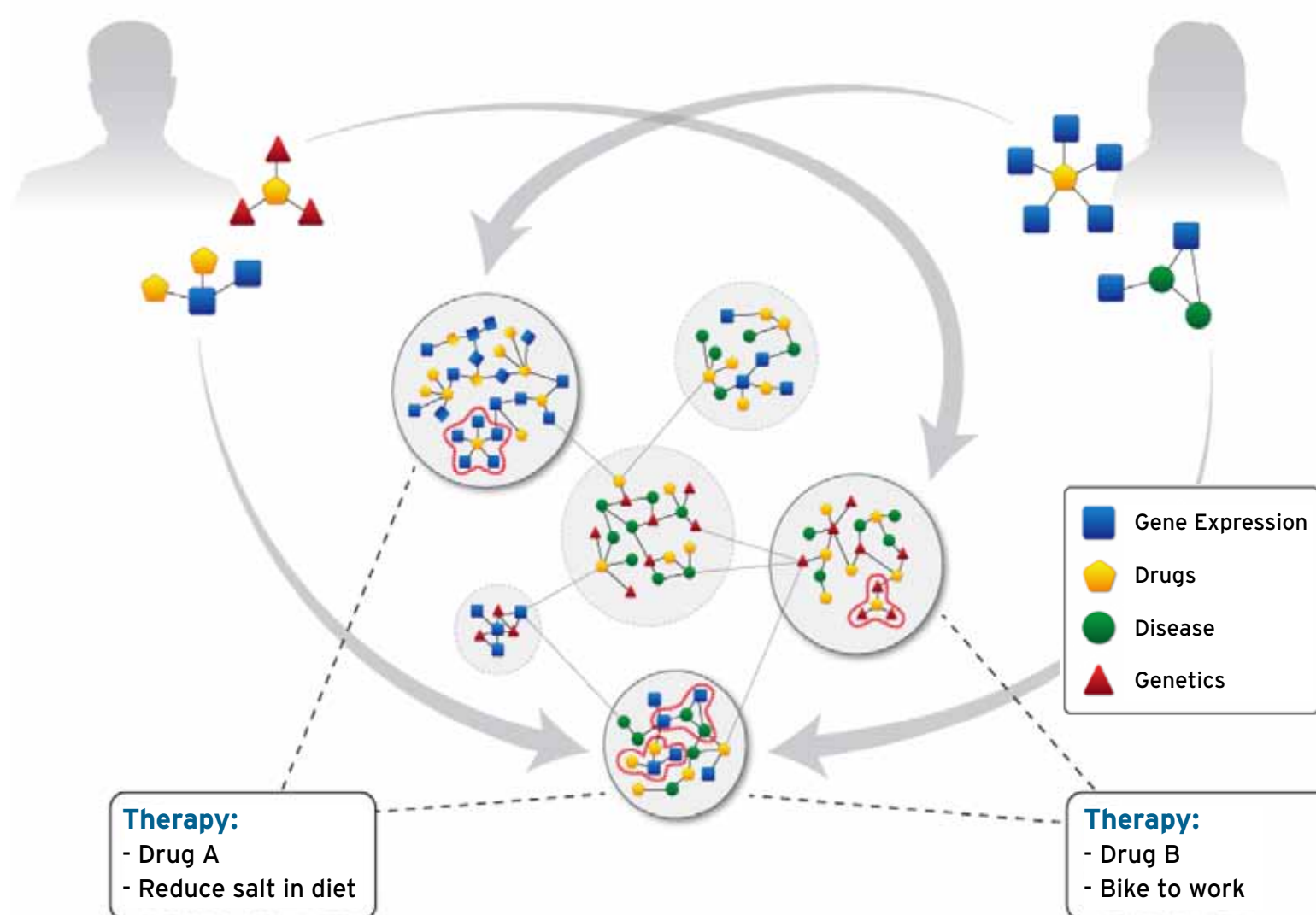
Other institutions will help us validate or invalidate different aspects of the models of disease we develop. We will use that feedback to refine and evolve our models, and then put them back into the community for further testing. This collaborative approach—which has been used in theoretical particle physics, climatology, and even economics—involves seeking out multiple iterations from numerous scientists around the world, and will lead to the best possible models of disease. Ultimately, these models will be a detailed reference for interpreting molecular measurements in individual patients and planning clinical interventions (see Figure 2).

» **Mount Sinai is one of only a handful of research institutions around the country focusing on computational biology in genomics. Why is it critical to the future of human health that other places follow Mount Sinai's lead?**

As we move away from single genes and into networks, the complexity increases exponentially, and the scales of data we generate will exceed everything that is in the digital universe today. The only way to understand such vast scales of information is by employing advanced mathematical algorithms, which are executed on super computer resources. Patients will seek out institutions that have the most knowledge about their disease. As a result, medical centers that do not focus on computational biology will fall behind.

» **Mount Sinai's genetics department is one of the largest in the country. Led for many years by Robert Desnick, MD, PhD, Dean of Genetics and Genomics, the department is credited with remarkable discoveries like the developing enzyme replacement therapy for devastating rare genetic conditions such as Fabry disease and Niemann-Pick B disease. What do you hope to see the department accomplish over the next several decades?**

Dr. Desnick and his colleagues are among a mere handful of researchers in the world who have uncovered the cause of a disease, developed a treatment for the disease, and successfully helped bring that treatment to market. My hope for the department is to achieve the same kind of success in disease areas that are very common—and caused by entire networks of genes—such as obesity, diabetes, heart disease, schizophrenia, autism, and cancer.



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Eric E. Schadt, PhD, one of the world's foremost experts in computational biology, has been appointed Director of the Institute for Genomics and Multiscale Biology, Chair of the Department of Genetics and Genomics Sciences, and the Jean C. and James W. Crystal Professor of Genomics at Mount Sinai School of Medicine. The Institute is being set up in partnership with Pacific Biosciences of California (PacBio) where Dr. Schadt will continue to serve as Chief Scientific Officer.

An expert in large-scale sequence variation, molecular profiling, and clinical data in disease populations, Dr. Schadt's research has provided novel insights into how massive amounts of data can be used to understand the complexity of diseases and lead to more informed decisions about drug discovery. He has also contributed to a number of important findings on the genetic basis of diabetes and obesity.

In his dual role at Mount Sinai and PacBio, Dr. Schadt will oversee a hub of genomics research, which will be at the forefront of the revolution in genetics and genomic sciences, and ultimately change the practice of medicine. He will foster multidisciplinary collaboration in areas such as newborn screening for rare genetic disorders, infectious diseases, and cancer.

Dr. Schadt is a founding member of Sage Bionetworks, an open-access genomics initiative. Before joining PacBio in 2009, he was Executive Scientific Director of Genetics at Rosetta Inpharmatics, a subsidiary of Merck & Co., Inc.