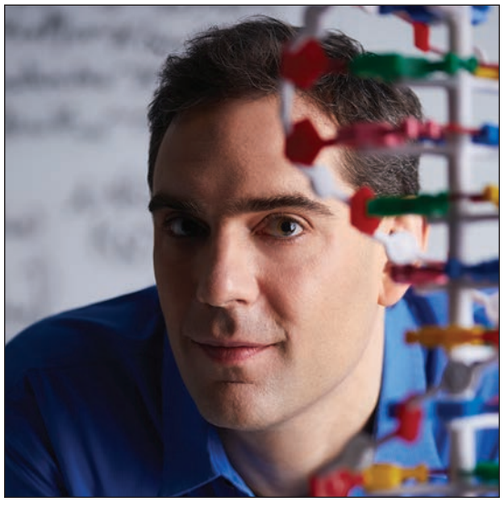
Precision Medicine



Adam A. Margolin

**An Interview with Adam A. Margolin, Ph.D.,
Professor and Chair, Department of Genetics and Genomic Sciences;
Director, Icahn Institute for Data Science and Genomic Technology; and
Senior Associate Dean for Precision Medicine, Icahn School of Medicine at Mount Sinai**

EDITORS' NOTE *Adam Margolin is a recognized leader in developing machine learning algorithms to analyze large-scale molecular datasets, to predict therapies specific for an individual patient, and to infer the key cellular processes that underlie cancer drug response. He is a passionate advocate of highly collaborative team-based research and has developed software systems to enable collaborative analysis for several of the largest national and international cancer, immunotherapy, and stem cell research projects. Before joining Mount Sinai, Dr. Margolin served as Director of Computational Biology and Professor of Biomedical Engineering with Oregon Health & Science University, where he led the University's computational research and software development programs. Earlier in his career, Dr. Margolin was the Director of Computational Biology at Sage Bionetworks in Seattle. He also worked at the Broad Institute of Harvard and Massachusetts Institute of Technology, leading a cancer genomics analysis program. Dr. Margolin earned his B.S. in economics from the Wharton School of Business at the University of Pennsylvania, his M.S. in computer science from the School of Engineering at the University of Pennsylvania, and his Ph.D. in Biomedical Informatics from Columbia University.*

INSTITUTION BRIEF *Mount Sinai Health System (mountsinai.org) encompasses the Icahn School of Medicine at Mount Sinai and eight hospitals that receive roughly 4 million patient visits annually. The Department of Genetics and Genomic Sciences is the 5th ranked genetics department nationally by Blue Ridge. The Icahn Institute for Data Science and Genomic Technology (datascience.icahn.mssm.edu) operates one of the largest supercomputing centers in academic research and one of the largest facilities for advanced genomic technology development. In 2014, the Institute was named by* Fast Company *as the 5th most innovative big data organization in the world.*

Will you provide an overview of the Department of Genetics and Genomic Sciences at Mount Sinai?

I lead the Department of Genetics and Genomic Sciences and the very closely-affiliated Icahn Institute for Data Science and Genomic Technology. Those two entities together are trying to drive the future of precision medicine by utilizing highly advanced data analytics integrated with advanced genomic technologies. Our goal is to discover new therapies and bring those therapies to patients faster than has ever been possible.

How much of an impact is the concept of precision medicine going to have on revolutionizing the delivery of customized healthcare?

If Floyd Mayweather went into a boxing match with just a strategy of "I'll throw a right uppercut and knock the other guy out in the first five seconds", that would be pretty risky. Rather, he has an arsenal of weapons and the ability to apply them at the right moments to counteract his opponent's tricks. And he went 50-0.

Similarly, for a disease like cancer, almost nobody believes there will be one or two silver bullet cures. Rather, cancers utilize many molecular tricks to evade all of the body's mechanisms to hold uncontrolled cell growth in check. Each cancer uses a different set of tricks which even evolve over time to employ new tricks to get around therapy. We need to continue to understand all of these tricks so we can build our arsenal of weapons against them. We need to quickly identify each trick so we can apply the right weapon to weaken the cancer, and apply another weapon as the cancer evolves, until we knock the cancer out or run out the clock and win by decision. We don't need a single knockout punch. We can go undefeated with this strategy.

Is there close collaboration across the health system in this process?

We need more than just collaboration. We need to work together to pursue big, ambitious goals that can only be accomplished by teams of experts sharing insights and information in real time. Academic institutions are structured such that individual researchers typically wall off information for periods of years until they can claim credit for any insights through a publication. This model does not work in the big data era. When a funder gives millions of dollars to an institution, it is very likely these resources will be funneled towards building up the name of one or a few researchers, and will not catalyze the key synergies needed to make real progress.

We're going to flip this antiquated model on its head. In collaboration with the company Sema4, we are planning to generate one of the largest existing cancer genomics datasets, including whole exome, whole transcriptome and germline sequencing for thousands of consented patients per year. All of this data will be immediately available to anyone at Sinai, and publicly available as soon as possible. We will integrate this data with data from tens of thousands of additional patients available from public sources. We will attract the best people in the world at developing technologies for measuring previously undetectable key molecules within disease samples and data generated by them will be immediately available to everybody. We will attract the top data scientists who can identify key patterns from massive amounts of data. These people will come from across industries – people like me, who will make the choice to forgo lucrative opportunities such as in data analysis for a hedge fund, and apply the same data science skills to biomedical research. And all of their analytical insights will be immediately available to everybody.

At the same time, we will develop new technologies that allow a tumor to be taken out of a patient's body and grown in a dish. Then we can test the tumor's response to many drugs or genes targeted by CRISPR. Results from these experiments will be available to everybody. By working as a large team that shares all information in real time, we will continuously iterate between generating novel molecular data quantifying disease, applying sophisticated analytic methods to predict novel drugs and drug targets, and testing these predictions on samples that recapitulate a patient's response to therapy. Each area of research will continuously learn from results generated by the others, creating flywheels of innovation that eventually allow us to triangulate on the most effective therapies that can be brought to benefit individual patients.

I will not put my name in the lead role for any of this work in any academic publication. Academics think that scientific leadership means getting primary credit for major projects. That's not leadership. It's the opposite of leadership. We will pursue new ways of working geared towards the modern era of big data and advanced technology driven research. We will pursue big ambitious goals that can only be tackled by harnessing everyone's best contributions, while allowing each individual to succeed by building on the work of others. I won't take credit for any of it. But we'll change the world. ●