DRS. ROBERT AND ROSALIND WRIGHT ARE A VISIONARY TEAM IN THE ULTIMATE TEAM SCIENCE: EXPOSOMICS

THE PROMISE OF THE EXPOSOME

BY ALISON DALTON

You've probably never heard the term "exposomics," but many researchers consider the field to be nothing less than the future of medicine. And with Drs. Robert and Rosalind Wright at the helm, Mount Sinai will soon be at its forefront.

Exposomics is the missing piece of the puzzle that will allow us to predict who will get sick—and to intervene to prevent that from happening. Just as the Human Genome Project identified and mapped the totality of human DNA, exposomics seeks to measure the totality of human environmental exposures: the exposome.

"Mount Sinai is already leading the way in population genomics," says Robert Wright, MD, PhD. "We came here to position Mount Sinai as a world leader in population exposomics. With the successful integration of the two, Mount Sinai will be at the forefront of understanding how genes and environment interact, which is exactly how biology works. Genes and environment don't act independently, so we have to stop researching them as if they do."

If anyone is qualified to lead the way into the future of medicine, it's Drs. Robert and Rosalind Wright. Recruited from Harvard Medical School in 2012, the Wrights wield unique transdisciplinary expertise spanning fields as diverse as pediatrics, internal medicine, toxicology, neurodevelopment, pulmonology, developmental and lifecourse epidemiology, exposure science, psychophysiology, epigenetics, molecular biology, and pulmonary and critical care medicine.

Rosalind Wright, MD, MPH, formerly on the clinical and research faculties at Harvard Medical School and the Harvard School of Public Health, is now the Horace W. Goldsmith Professor in Children's Health Research and Dean for Translational Biomedical Research at the Icahn School of Medicine at Mount Sinai. Robert Wright, former Professor of Pediatrics at Harvard Medical School, is the Ethel H. Wise Professor of Community Medicine and Chair of the Department of Environmental Medicine and Public Health at the Icahn School of Medicine. →

THE MOUNT SINAI INSTITUTE FOR EXPOSOMICS

The Wrights came to Mount Sinai as part of a grand vision: The Mount Sinai Institute for Exposomics, the first institute for exposomics in the country and the world. The Exposomics Institute will bring together researchers and clinicians from many disparate areas of expertise and training—exposure scientists, chemists, social scientists, experts in geospatial health informatics and methods, epigeneticists, data scientists, and many others—to join in the exciting cross-fertilization that is team science.

"Dean Charney had the pioneering vision to bring scholars together in ways that foster constant cross-talk and create the ideal environment for the team science needed in exposomics," says Rosalind Wright. "That's why team science is so exciting and so successful: when you have those sorts of exchanges, interesting, innovative ideas inevitably happen.

"The best ideas and discoveries emerge when you bring together seemingly disparate areas of science and get different perspectives to address the same problem. Think of what we can do when we bring together environment and genetic experts to tackle the same health question," she says.

In the world of health care, great visions require significant investment. In their four and a half years at Mount Sinai, the Wrights have brought in an astonishing $75 million in new funding from the National Institutes of Health under the Children's Health Exposure Analysis Resource (CHEAR) and Environmental Influences on Child Health Outcomes initiatives, and an NIH Core Center grant. Mount Sinai received the largest CHEAR grant of any institution in the country.

The complexity of measuring the exposome surpasses even the challenge of measuring the human genome, says Robert Wright. "Scientists in the Human Genome Project knew there were roughly four billion base pairs that had to be mapped—a huge task, but a finite one. With exposomics, even knowing where to stop is extremely difficult.

"Some scientists outside the field say, 'You can't possibly measure everything that happened to someone,'" he continues. "That may be true, but as we move closer to being able to measure the totality, the better we'll understand why one person becomes ill and why another person does not."

Exposomics is big data, and taking on the challenge of measuring the exposome is possible because of existing resources such as Mount Sinai's $3 million supercomputer, Minerva. Population exposomics generates millions of data points. Because Mount Sinai has invested heavily in bioinformatics and computer science, it has the computing capacity right now to manage that kind of big data.

Integrating exposomics into the Mount Sinai Health System is a critical partnership because environment can be modified, unlike genetics. Exposomics is crucial to the new, evolving health care system model. From a long-term financial perspective, understanding where you can intervene to prevent illness is going to be more profitable than treating disease.

Says Robert Wright, "Dr. Davis and Dean Charney have invested in exposomics because they have the vision to see that the future financial rewards in health care are going to lie in keeping people out of the hospital and exposomics will help us achieve that goal."

ENVIRONMENT: THE MISSING PIECE OF THE DISEASE PUZZLE

Although enormous advances have occurred, genomics hasn't turned out to be the panacea for explaining why complex diseases like autism, obesity, or asthma occur. At most, only 25 percent of these types of diseases can be explained by genetics alone. This is not surprising, as genes don't change: they are exactly the same on the day one dies as they were on the day one was conceived.

Environment is the missing piece of the disease puzzle. DNA doesn't work in isolation; the quality of the air we breathe and the food we eat interacts with our genes, and together they determine our health. Even "purely" genetic diseases are affected by environmental exposures. Cystic fibrosis, for example, is exacerbated by air pollution and allergens.

Environmental exposures include everything from chemical exposures, such as lead and air pollution, to social factors, such as stress and availability of nutritious food. In exposomics, the Wrights are developing methods to gather data on all these environmental factors from numerous, and sometimes surprising, sources: placental tissue, baby teeth, NASA satellites, and even brain tissue donated from the deceased. To do exposomics well requires reconstructing the past environment, similar to the way forensic scientists piece together events.

Just as in forensics, exposomics needs to understand when events happen. This is because the human body's vulnerability to toxic exposures varies over time, a concept known as "critical windows of vulnerability."

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Some of the most critical windows to exposure occur in early childhood, even in the womb. Exposures during those periods can lead to disease years or decades later. However, researchers now know that individuals are also more vulnerable at other life stages, such as adolescence or later in life. Exposomics needs to study these effects across these life stages.

As an example, exposure to air pollution at age one may produce asthma at age eight, while exposure at age three to those same pollutants may not. Rosalind Wright's research has already shown that eating a diet high in antioxidants and certain other nutrients during pregnancy can mitigate toxic effects of air pollutants or stress on a child's developing brain.

EXPOSOMICS IN MOUNT SINAI'S NEIGHBORHOOD

Certain communities, like certain individuals, may be sicker than others. In many cases this is because they have different environments, such as more traffic-generated air pollution, more industrial pollution, and more poverty-related stress such as crime or violence. Exposomics is the key to understanding health disparities.

"We sit at the border between some of the wealthiest communities in Manhattan and some of the poorest neighborhoods," says Robert Wright. "Mount Sinai has long had a mission of helping the underserved, particularly in its immediate vicinity, and it has the vision to understand that exposomics can aid all communities, but in particular those communities disproportionately burdened by environmental pollutants and social stressors."

Adds Rosalind Wright, "At Mount Sinai, the research institution is built around the hospital, enhancing the opportunities to translate the research back to patient care more readily. That was a key component that caught our attention and drew us from Harvard to Mount Sinai. At Mount Sinai we have a better opportunity to translate the research back to patient care more readily."

At her East 98th Street laboratory, the Physiological Assessment of Children's Environmental Risk Laboratory, Rosalind Wright's research extends to meaningful interventions. Her team has shown that stress in pregnancy can negatively affect an unborn child's later biological responses to stress, putting them at risk for diseases such as asthma or obesity. Notably, her research has also shown that sensitive caregiving in the first year or two after birth buffers those later health effects. This knowledge has prompted a clinical initiative: Dr. Wright is currently implementing a program through the Mount Sinai Parenting Center to enhance parents' caregiving skills, in hopes of diminishing adverse health outcomes, including asthma, in early childhood.

WORKING AS A TEAM

Though they didn't start that way, the Wrights now work closely together. Both grew up in Michigan and attended the University of Michigan Medical School, where they met. "Our training backgrounds are actually quite different, so collaboration didn't seem natural at first. But in many cases we were studying the same health outcomes, but from different perspectives. That's when we started to understand the value of interdisciplinary research. We talk a lot and we share ideas," says Rosalind Wright. "A lot of people have asked us how we make that kind of closeness work," she laughs. "We're together because of the big-picture team, but we don't overlap in our expertise, necessarily. It's synergistic.

"It's very exciting to us that health disparities can be addressed through exposomics," she adds. "We realized at some point that through research we could move the needle more. But ultimately we want the research to result in better health outcomes. We're physicians. We want this to translate."

ENABLING TECHNOLOGY
BIOINFORMATICS

What Your Baby Teeth Can Tell You

What do big data and tiny teeth have in common? Research leaders at Mount Sinai have found that prenatal exposure to certain metals, such as lead, during critical periods of development, coupled with a lower uptake of the minerals manganese and zinc—essential elements for healthy development—may be linked to autism. They made this discovery by examining the spatial patterns of metals in the deciduous teeth (commonly called "baby teeth") of twins at established stages of prenatal development. Employing laser-based chemical analysis and bioinformatics methods known as Bayesian statistics, they reconstructed past exposures using mathematical algorithms. Babies with autism spectrum disorder absorbed more lead than their healthy twins during identifiable timeframes in their development. The ability to identify past exposures has significant implications for future research, including, potentially, the development of a diagnostic tool employing the analysis of tooth-based biomarkers to predict risk for neurodevelopmental disorders, and methods to monitor and prevent exposure to metals shown to be harmful during critical windows of development.