CONNECTING THE DOTS

BETWEEN HEART DISEASE AND FULL-BODY HEALTH

BY BARBARA BRODY

he heart is undeniably among
the most crucial of organs: When
its ability to send blood, oxygen,
and other nutrients throughout
the body becomes compromised, nothing
else works as it should. Yet the traditional approach to studying and managing
cardiovascular disease has been fairly
narrow. Both clinicians and scientists have
paid almost exclusive attention to inflammation and atherosclerotic plaque in the
arteries along with structural and electrical
abnormalities within the heart itself.

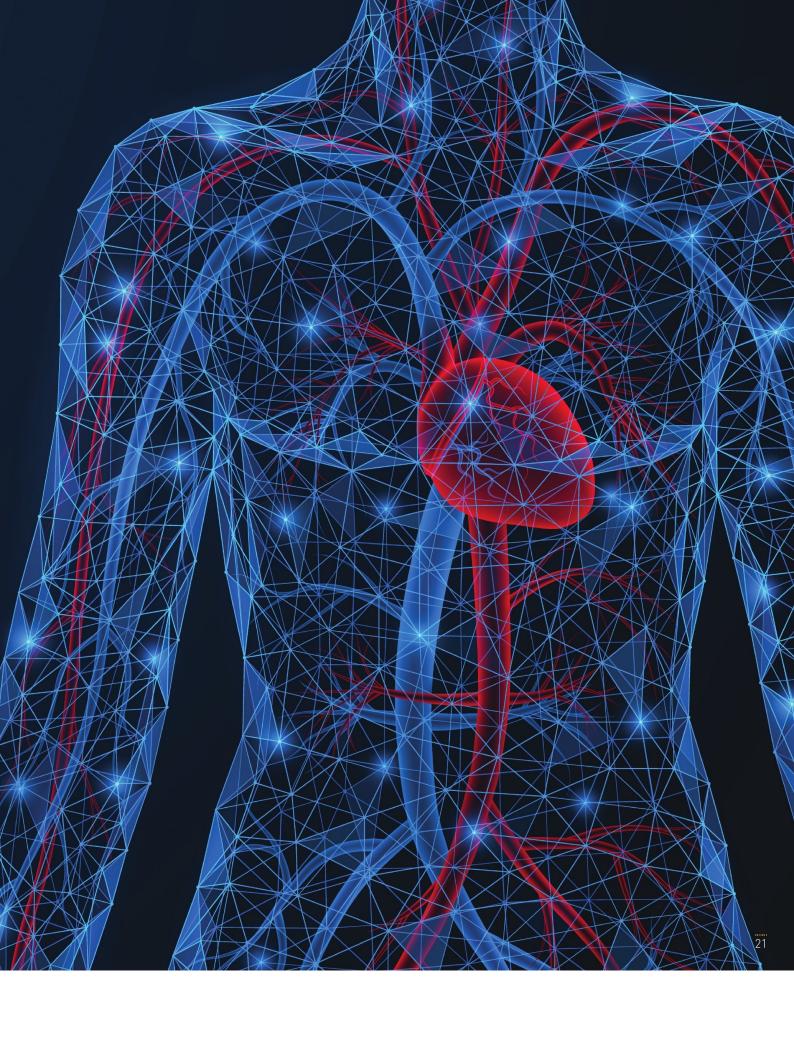
Filip K. Swirski, PhD, Director of the new Cardiovascular Research Institute (CVRI) at the Icahn School of Medicine at Mount Sinai, takes a far broader perspective. By delving into how the cardiovascular system interacts with every other major body system, he is developing a more thorough understanding of what it means to be heart healthy—and how to live well for as long as possible.

"The vascular system does not exist in isolation. We must branch out and understand how the vasculature of the heart really participates with other systems," says Dr. Swirski, who is also the Arthur and Janet C. Ross Professor of Medicine (Cardiology), and Professor of Diagnostic, Molecular and Interventional Radiology at Icahn Mount Sinai. "We are only going to gain limited insight if we restrict ourselves to just looking at the heart or just the blood vessels."

A renowned leader in cardiovascular immunology research, Dr. Swirski served as

a professor at Harvard Medical School and a principal investigator at Massachusetts General Hospital before coming to Mount Sinai a year ago to launch CVRI. Since then, he has been building an interdisciplinary team that includes experts in immunology (his own area of expertise), neurology, and metabolism.

"Science really requires collaboration," he says, adding that Mount Sinai—which has long encouraged experts to avoid working in silos—is already a global leader in clinical cardiology. The new CVRI will be integrated under Mount Sinai Heart, which aims to advance both fundamental and translational science across three key areas: lifestyle and disease prevention, systems physiology and bioengineering, and genetic medicine.



MOVING BEYOND DIET AND EXERCISE

Approximately 80 percent of cardiovascular disease is believed to be preventable, yet heart disease remains the leading killer worldwide. Why? While experts have long known that high blood pressure, high cholesterol, hyperglycemia, and obesity play major roles, these and other risk factors have often been studied independently, Dr. Swirski notes. Investigating them in context with one another will give scientists greater insights into how one's overall lifestyle impacts physiology.

Additionally, scientists at CVRI are poised to uncover findings that go far beyond the typical "eat less, move more" platitudes. They are exploring nuances such as whether the time of day someone eats a specific food is important and whether good stress—the kind you might feel on a first date or when a promotion lands you just slightly out of your comfort zone—is beneficial or detrimental to the heart and blood vessels.

"It's a much richer way of studying biology and a very important line of investigation," Dr. Swirski emphasizes. CVRI is also delving into lesser-known potential cardiovascular risk factors, such as sleep patterns and the composition of the gut microbiome.

EXTENDING BRIDGES ACROSS DISCIPLINES

At CVRI, systems physiology and bioengineering research is all about studying cardiovascular disease in the context of other body systems. This requires close coordination between specialists in immunology, hematology, neuroscience, biochemistry, endocrinology, and vascular biology.

Dr. Swirski describes the blood vessels as a highway through which blood, cells, and signaling molecules travel, as do inflammatory substances. Inflammation is strongly associated with heart disease and stroke, yet the origins of inflammation in a particular patient—as well as why the body doesn't always dampen an inflammatory response when it should—are not always clear.

Dr. Swirski's team also wants to understand how inflammation might protect against or contribute to infectious and neurodegenerative conditions. "We cannot understand the blood and the heart if we don't understand metabolism, if we don't understand the nervous system, if we don't understand the endocrine and immune systems, and so forth," he explains.

The type of research CVRI is conducting requires "engaging in areas where you may not have much expertise," says Dr. Swirski. "But this is actually one of the reasons why Mount Sinai is an attractive place to do this kind of work." While he is an authority in immunology, he admits that there has been a learning curve as he has recently ventured into less familiar fields. Close coordination with various Mount Sinai leaders—including neuroscientist Scott J. Russo, PhD; biomedical engineer Zahi A. Fayad, PhD; and Miriam Merad, MD, PhD, an expert in precision immunology, hematology, and

oncology—has proven immensely helpful.

Eight different laboratories, including Dr. Swirski's own lab, are dedicated to taking a systems physiology and bioengineering approach to studying cardiovascular disease. These groups of scientists are striving to illuminate the complex ways by which the heart communicates with other organs and body systems. The teams are employing a variety of techniques, including tissue and organoid engineering, gene editing for disease modeling, and computational modeling, and they are also developing new biomedical devices.

UNDERSTANDING GENETIC PATHWAYS AND DEVELOPING GENE THERAPIES

Why do some people develop serious cardiovascular disease despite remaining physically active, not smoking, and eating a diet that enables them to maintain a "normal" body mass index? Clearly, genetics

