Cardiovascular health isn’t just about the heart, or about the thousands of veins, arteries and capillaries that provide oxygen and other nutrients to every corner of the body. According to Clyde Yancy, MD, MSc, the Magerstadt Professor and chief of Cardiology in the Department of Medicine, cardiovascular health involves an extraordinarily complex set of inputs that modern medicine has just begun to unravel. “It’s not just an inciting stimulus and then a disease, but it’s the aggregate,” said Yancy, who is also vice dean of Diversity and Inclusion and a professor of Medical Social Sciences. “It’s the environmental exposures, risk factors that impact biology and anatomy, and genetic predisposition to vulnerability. All of these things come together in an intricate manner that is redefining cardiovascular disease.”

Discovering those variables and the subsequent contribution to disease is challenging, but translating those discoveries into concrete medical practices that can improve patients’ lives is is exciting, maybe even transformational, which is why the American Heart Association (AHA) Strategically Focused Research Networks (SFRN) are an important vehicle for bench-to-bedside-to-bench discoveries at Feinberg. “It’s not the traditional granting mechanism to the sole investigator, but rather a process iteration and development that is intended to align a group of investigators toward one research focus,” Yancy said. “The successfully funded research networks generate an intense spirit of discovery, combined with the tool of collaboration — that makes these networks and the consequent discoveries very important.”

The AHA recently awarded Northwestern a sixth SFRN, the most at any institution in the country. The SFRN centers have investigated a range of topics, such as the arc of cardiovascular risk from childhood to adults and the dense explanations of health disparities, and new centers are utilizing cutting-edge technology to ask fundamental questions about conditions such as atrial fibrillation and sudden cardiac death. Mercedes Carnethon, PhD, the Mary Harris Thompson Professor and vice chair of Preventive Medicine in the Department of Medicine, is a veteran of three centers: one aimed at preventing cardiovascular disease, the other focused on cataloguing the impact of health disparities and another on the debilitating impact of vascular disease in the lower extremities.

In the prevention network, scientists including Carnethon and Norrina Allen, PhD, associate professor of Preventive Medicine in the Division of Epidemiology and of Pediatrics, showed that periods of poor cardiovascular behavior are followed by poor cardiovascular health, across populations and in younger patients than ever before.

The disparities network made similar discoveries, showing how markers of poor diet influence kidney function and cardiovascular health far into the future.
AHA and Northwestern (continued from cover page)

“Unfortunately, many of these poor behaviors and exposures are more common among lower-income populations and non-whites,” said Carnethon, who is also chief of Epidemiology in the Department of Preventive Medicine.

The multidisciplinary nature of these centers was a boon for team science, according to Carnethon.

“It is a useful mechanism because it supports approaching a problem from multiple perspectives — basic, clinical and population science,” Carnethon said. “There are few mechanisms that would allow for such a comprehensive approach to investigate a single problem.”

While several current centers continue to make progress in cardiovascular disease prevention, newly awarded centers are exploring other, less-studied conditions.

Atrial fibrillation, an erratic or quivering heartbeat that results in abnormal blood flow in the heart, is the most common abnormal heart rhythm in adults. According to Rod Passman, MD, the Jules J. Reingold Professor of Electrophysiology and principal investigator of the SFRN studying the condition, atrial fibrillation is a major contributor to stroke, dementia and heart failure, but questions remain about its origin and optimal treatment.

To develop new treatments or diagnostic methods, the group is taking on a foundational, chicken-or-egg-type problem.

“We are trying to understand whether it’s the rhythm of the heart that causes these problems, or is it that people who have abnormal rhythms also have other structural abnormalities that may predispose them to the consequences of atrial fibrillation,” said Passman, who is also a professor of Medicine in the Division of Cardiology and of Preventive Medicine.

Passman is leading a project to normalize the rhythm of patients’ hearts using ablation, following up several months later with 4D flow MRI to see if correcting the rhythm has favorably impacted the structure of the heart and blood flow in the upper chambers.

“If we can take patients with abnormal flow and turn that flow normal by normalizing the rhythm, it would show you that the rhythm abnormality is the cause,” Passman said. “If we don’t change it, it suggests the abnormal rhythm is just some sort of epiphenomenon, and we should be looking at other sources of stroke beyond atrial fibrillation and not wait for the abnormal rhythm to occur before instituting treatment.”

The goal of this project, and others in the SFRN, is to help develop technologies that can identify patients at risk for atrial fibrillation, so clinicians can intervene before serious illness strikes. This is particularly important for atrial fibrillation, as many patients’ disease lies in wait, largely undetectable until a major stroke or other illness, according to Passman.

“In many patients, stroke is the first manifestation of the disease — we didn’t know that anything was wrong before,” Passman said. “This is the beginning of trying to find an earlier pathologic mechanism, and advances like this don’t happen in a vacuum. If you want to make a significant change, you have to take something from the bench to the bedside.”

Another disease with a largely unknown etiology is sudden cardiac death and arrhythmias, according to Elizabeth McNally, MD, PhD, the Elizabeth J. Ward Professor of Genetic Medicine, is leading a newly awarded SFRN that will examine how it intertwines with more pedestrian heart arrhythmia.

“Even with all the rapid advances in the genetics of arrhythmias, there are still many patients for whom we do not find clear-cut mutations,” said McNally, who is also director of the Center for Genetic Medicine, a professor of Medicine in the Division of Cardiology and of Biochemistry and Molecular Genetics. “This is because we don’t yet know all the genes and, in some cases, the risk is correlating with having combinations of gene variants.”

Feinberg scientists will use genetic data from patients who have experienced sudden cardiac death and arrhythmias, running large-scale analyses to tease out how these conditions are related, before moving to test the impact of variants in stem cell models of heart tissue.

“These cell models of heart disease are very powerful, and we have the capacity to measure arrhythmias in the models,” McNally said. “They will not only help us better define the genetic risk, but ultimately these models will become important platforms in which we can test new therapies.”

Further, while genetic testing is becoming more commonplace, the application of that information is uneven because many clinicians don’t have the proper training and there’s a relatively thin databank of genetic information from historically understudied populations, according to McNally.

“An especially pressing need is to get better at interpreting variants of uncertain significance in diverse populations, where there are more variants of uncertain significance and inadequacy,” McNally said. “We also hope to address the provider-side knowledge gap in genetics with provider education.”

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