

THE HEART INSTITUTES AT NORTHWESTERN MEDICINE  
FEINBERG CARDIOVASCULAR RESEARCH INSTITUTE

# CARDIOVASCULAR REPAIR AND REGENERATION

## A Collaborative Approach to Advancing Cardiovascular Medicine

At the Feinberg Cardiovascular Research Institute at Northwestern Medicine, we are advancing the therapeutic use of endothelial progenitor cells (EPCs)—a special type of stem cell originating from blood and bone marrow—and developing new drugs for the treatment of cardiovascular diseases. A small number of EPCs can be found in the blood of healthy individuals, but most reside in the bone marrow. In response to cardiovascular injury, endothelial and other progenitor cells are released from the bone marrow into the blood and travel to the injury site where they contribute to the growth of new blood vessels (a process called neovascularization) and to repair of the heart muscle itself.

### Why are Endothelial Progenitor Cells Important in Cardiovascular Disease?

Patients with fewer circulating EPCs are less likely to recover from cardiovascular disease, or their recovery may be limited. The number and function of EPCs can be reduced by many of the same factors that increase the risk for cardiovascular disease, including hypercholesterolemia, cigarette smoking, Type 2 diabetes mellitus, kidney disease, and aging. Conversely, strategies for improving cardiovascular health, such as exercise and treatment with statins or growth factors, increase the number and functional activity of EPCs.

Recent clinical data suggest that EPCs can be safely collected from a patient's own blood and transplanted to regions of the patient's heart or limbs to improve blood flow and reduce the symptoms associated with cardiovascular illness. However, despite these promising early results, the effectiveness of cell therapy is often less than optimal because cells collected from older patients with multiple cardiovascular disorders are less potent and comparatively scarce, and because very few of the transplanted cells are retained and survive in the injured tissue. Technologies that overcome these limitations must be developed to ensure that patients receive the maximum possible benefit from cell therapy.

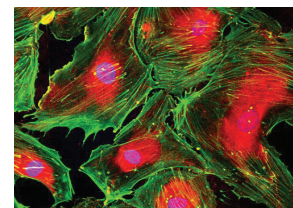
At the Feinberg Cardiovascular Research Institute at Northwestern Medicine, our investigators are collaborating across Northwestern University to conduct a series of individual studies on the mechanisms associated with endothelial progenitor cell fate, function, and dysfunction. The goal is to develop new approaches and strategies for the prevention and treatment of cardiovascular disease. Our researchers offer unique skills and expertise in areas essential for our success: vascular biology and fibrosis; vascular and stem cell biology; mitochondrial biology; and the mammalian fibrinolytic system. Through this University-wide model of collaboration, we have the opportunity to engage and maximize the talents of the broader Northwestern University research community.



"My colleagues and I at Northwestern Medicine are excited to be leading breakthrough studies that center on developing approaches and technologies that can improve outcomes for patients with cardiac and vascular disease, including congestive heart failure."

Douglas Vaughan, MD, Irving S. Cutter Professor and Chair, Department of Medicine

*The following priority studies are focused on improving our knowledge of how endothelial progenitor cells stimulate vessel growth or on developing techniques that maximize their effectiveness for treating cardiovascular disease.*



Endothelial progenitor cells

## Areas of Research

### **Peptide Amphiphiles to Augment Progenitor Cell Therapies – Exploring the uses of novel bioactive nanopeptides for increasing the potency of EPC-based therapies**

The overall goal of this research area is to develop innovative, therapeutic approaches for advanced cardiovascular conditions, such as congestive heart failure, with the use of novel, bioactive nanopeptides to augment the potential of endothelial progenitor cell-based therapies. The successful completion of the studies will position us to move forward with human applications of these novel approaches to treat otherwise untreatable cardiovascular disease. Principal Investigator, Tsutomu Kume, PhD, has expertise in the development of the mammalian cardiovascular system and Project Leader, Sam Stupp, PhD, Director of the Simpson Querrey Institute for BioNanotechnology, has extensive experience in the development of novel biomaterials.

### **Role of PAI-1 in Cardiovascular Repair and Fibrosis – Characterizing how the fibrinolytic cascade contributes to EPC mobilization, function, and fate**

The overall goal of this research area is to investigate the role of PAI-1 in cardiac repair and fibrosis. PAI-1, or Plasminogen activator inhibitor-1, is considered a critical regulator of the fibrinolytic system. It is anticipated that we will identify and define the direct links of PAI-1 with endothelial progenitor cell mobilization and the molecular pathogenesis of cardiac fibrosis. With these insights, we are already testing novel targeted therapies that appear to slow the rate of vascular aging while simultaneously addressing fibrogenic processes to prevent and treat end-stage heart disease. Principal Investigator, Douglas Vaughan, MD, Irving S. Cutter Professor and Chair, Department of Medicine, is a leading authority in the study of vascular biology and fibrosis.

### **Mitochondrial Defects in EPCs in Diabetes and Aging – Studying the mechanisms responsible for the impaired function of EPCs in elderly patients and patients with diabetes**

The overall goal of this research area is to determine the mechanism for the impaired function of endothelial progenitor cells in diabetes and older patients, and to enhance the therapeutic potential of these cells. Understanding the effects of diabetes and old age on endothelial progenitor cell function may potentially lead to the improvement of their angiogenic potential and better treatment of ischemic heart disease. Principal Investigator, Hossein Ardehali, MD, PhD, has performed pioneering research in the fields of mitochondrial biology and reactive oxygen species.

### **Epigenetic Modulation of EPCs for Cardiomyogenesis – Investigating how epigenetic reprogramming can enhance the potency of EPC for myocardial repair**

The overall goal of this research area is to explore the feasibility of endothelial progenitor cell reprogramming by chromatin remodeling in order to improve their function and cardiomyogenic plasticity. The proposed studies, if successful, will have a significant effect on the improvement of already approved clinical cell therapy for myocardial repair and regeneration. Principal Investigator, Raj Kishore, MD, is an expert in vascular and stem cell biology.