New research discovers genetic defect linked to African Americans with heart failure

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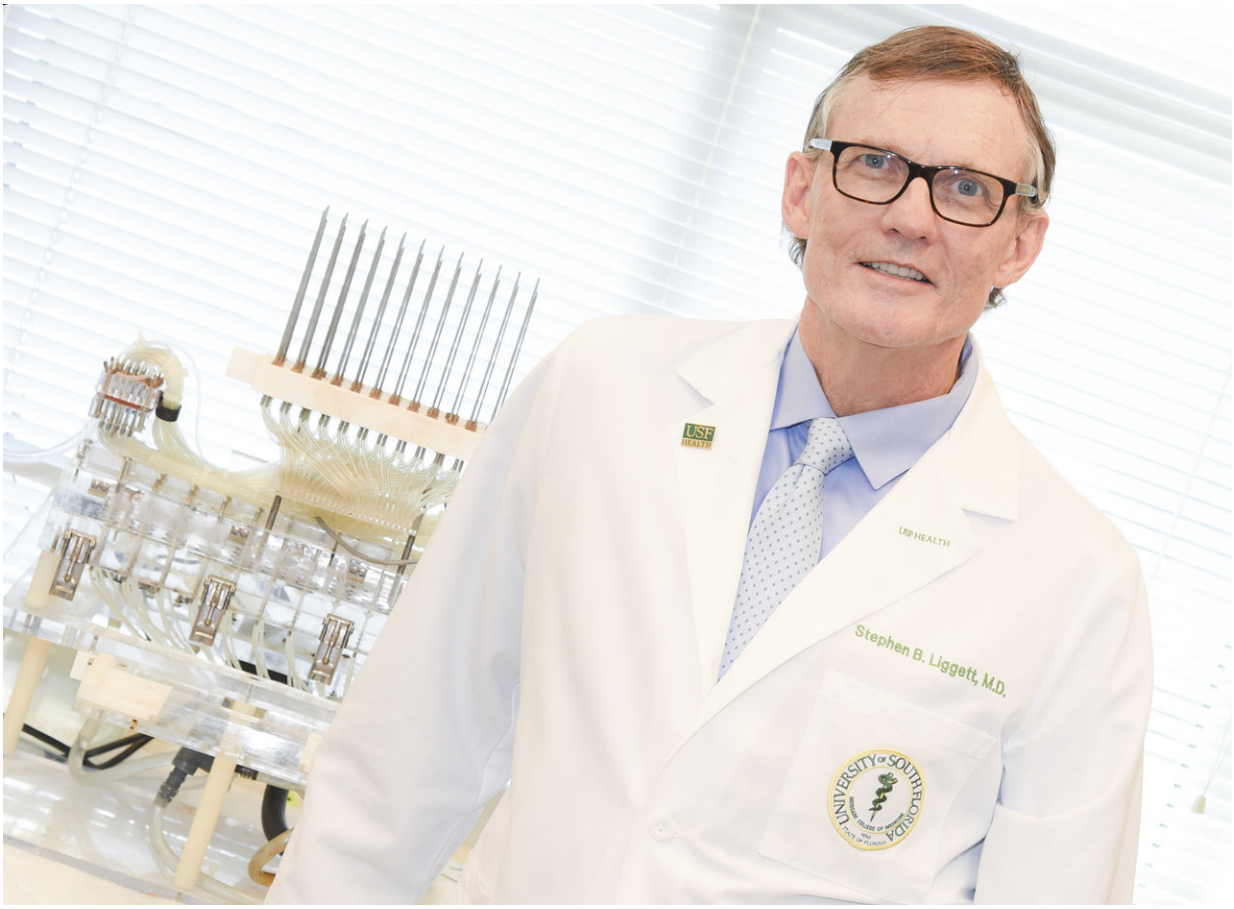

Stephen Liggett, MD, professor of internal medicine and vice dean for research at the University of South Florida Morsani College of Medicine, Tampa, Fla., led the first genetic study of its kind to examine the genetic basis of heart failure in African Americans. Credit: University of South Florida

Heart failure is more common, develops earlier and results in higher rates of illness and death in African Americans than in whites.

Now, the first genetic study of its kind to examine the genetic basis of heart failure in African Americans, led by the University of South Florida (USF), Tampa, Fla., has identified a genetic defect linked specifically to heart failure in this population. The discovery could lead to more precise and effective treatments for African Americans, who are more likely to suffer from a common form of heart failure of unknown cause called idiopathic dilated cardiomyopathy (IDC). IDC is a condition in which the heart weakens, cannot pump blood properly and becomes progressively enlarged.

The study was published Feb. 26 in the *Journal of Personalized Medicine*.

"We know that this form of heart failure has a worse prognosis in African Americans and does not respond as effectively to most therapies as compared to the same treatments in Caucasian individuals of European descent. Yet, there had never been a genome-wide association study performed exclusively in African Americans," said senior author and project director Stephen B. Liggett, MD, professor of internal medicine and vice dean for research at the USF Health Morsani College of Medicine.

"We undertook this study because of the severe under-representation of African Americans in these types of trials, and, our idea that the genetic causes might be different in this population," Dr. Liggett added. "Our genome-wide analysis suggests that is indeed the case, and we may need to develop new drugs to target IDC in African Americans."

The Genetics of African American Heart Failure consortium examined genetic variations in the genomes of 662 African-American patients

recruited from five U.S. academic medical centers: the University of Cincinnati College of Medicine, Duke University School of Medicine, Johns Hopkins University School of Medicine, University of Maryland College of Medicine, and the Virginia Commonwealth University School of Medicine. All the study participants had no history of heart attacks and were diagnosed with IDC.

The researchers found that a variation in one gene, called CACNB4, could contribute to causing IDC in African Americans. That same genetic defect has not been found in white patients with IDC. More study is needed, Dr. Liggett said, but CACNB4 plays a key role in regulating calcium signaling important for cardiac muscle contraction, so a variation that interferes with the gene's function may lead to diminished pumping of blood by the heart.

In addition, variations in other genes suggested an association with IDC in individuals with African-American ancestry. So, the researchers mapped the biochemical pathways of these 1,000 genes, which created a network indicating the potential action by which these variations lead to IDC, and possible targets for new drugs. The consortium's analysis showed that genetic variations in African Americans account for 33 percent of the risk for IDC. And, many genes forming the pathway map were involved in how calcium regulates the work of heart muscle cells.

Dr. Liggett and his collaborators use various research methods, including examining genetic variation in different ethnic groups, with the aim of understanding how to best devise new drugs for treatment or prevention of heart failure. "Every time we perform these genetic studies, we learn something new and find another piece of the puzzle," he said, "Ultimately the dissection of this cardiovascular disease will lead to drugs that strike at damaging pathways with a high level of precision, resulting in personalized medicine for heart failure."

Nearly 6 million people in the United States have heart failure, a figure projected to increase to 8 million by 2030, according to the American Heart Association. The five-year mortality rates range from 30 to 50 percent, greater than for some cancers.

More information: Huichun Xu et al, A Genome-Wide Association Study of Idiopathic Dilated Cardiomyopathy in African Americans, *Journal of Personalized Medicine* (2018). DOI: 10.3390/jpm8010011

Provided by University of South Florida