Researchers present new theory that may lead to effective heart failure treatments

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Do the biological underpinnings of heart failure share more in common with cancerous tumors than other cardiovascular diseases? Research presented at American Heart Association meeting may show why heart failure treatments fail.

A team of Medical University of South Carolina (MUSC) researchers and cardiologists are presenting a number of studies at the American Heart Association conference that point toward new treatments for heart failure patients.

According to the American Heart Association, more than 5 million Americans are living with heart failure, and 550,000 new cases are diagnosed each year. It is a chronic disease that has no cure and typically worsens rapidly.

Dr. Francis G. Spinale and several other researchers from MUSC have put together scientific clues resulting in more than a dozen research studies on patients and mice that strongly suggest that a family of proteins called matrix metalloprotienase (MMP) play a crucial role in why the supporting tissue surrounding the heart, called the myocardium, goes through significant and deleterious effects in heart failure patients.

The conclusions reached by the team have already led to the development of a blood test for these MMPs. But more significantly, according to MUSC cardiac specialist Francis G. Spinale, MD, PhD, this research may demonstrate why current treatments for heart failure are

failing and point to novel treatment methods for heart failure patients, reduce the number of people on the heart transplant list and help prioritize those heart failure patients currently on the list.

Spinale said that this discovery dates back to the 1980s when he and colleagues observed microscopic changes and gross abnormalities in the tissues surrounding the hearts of patients with coronary artery disease. Naturally, Spinale wanted to know what caused these profound changes in these structures?

He found part of his answer in an unlikely place: an oncology conference.

"In early 90s I accidentally walked into a cancer conference and this oncologist was talking about how a tumor moves and invades normal tissue and he described these enzymes (later named MMPs) that chew and change the matrix of cell," he said.

"I put two and two together and theorized that these MMPs might play a role in some major cardiovascular diseases," he said.

Spinale and other researchers at MUSC then examined the hearts of transplant patients and discovered that these MMPs were significantly up regulated in heart failure patients. This was an observation that had eluded cardiologists for years because the number of MMPs in normal hearts is very low. Once heart disease sets in, there is a rapid and robust up regulation, he said.

"As a matter of fact, the MMPs in heart failure patients are very similar to those expressed in aggressive, malignant tumors which leads me to suspect that these MMPs are a pathologic group of enzymes that are expressed in disease progression in general," he said.

From these published discoveries, Spinale and his colleague, Dr. Michael Zile, developed a blood test to measure these MMPs in bloodstreams of patients so they could screen patients early in the disease. This allowed MUSC cardiologists to predict the progression of the disease and demonstrate a different signature of these MMPS in patients with different types of heart failure and guide us to a more personalized form of treatment.

"Indeed, we showed a very different MMPs profile exists in high blood pressure and heart failure than those patients with just a heart attack and heart failure," he said. We also assumed that in other cardiovascular diseases the MMP profiles would be different too. In fact, in thoracic aortic aneurysms, different MMPS emerge in the aortic wall and contribute to this disease."

Spinale said that his teams' MMPs research has implications for children and infants with heart failure. MUSC treats many children who require heart transplants

"We wondered if MMPs were observable in these children with heart failure who need transplants," he said. Surprisingly, we found a different and distinct MMP panel with these kids that suggest something in their programming is wrong. MMPs should be shut down but they continue to chew and degrade tissues."

This lead the MUSC team to consider that certain forms of heart failure are similar to cancer because these cells that are expressing MMPs are abnormal and express cancer-type enzymes.

"Perhaps we have been looking at heart failure treatment all wrong," he questioned. Perhaps there is a basic program that has been started in the body that is going wrong with these patients. Spinale theorized that this may explain why some of these drugs aren't working—they make

patients feel better but they don't slow the disease.

"We may have been looking at the wrong target."

Spinale said MUSC's research has several implications for the near future.

"These are still new results and starting to assimilate these new methods into clinical practice. The blood test we are working on is the first step and we can use this to more aggressively modify other risk factors—cholesterol, diet, exercise and medications. We would bring them back to the clinic more frequently to monitor the progression in the heart in much like you would do with a cancer patient."

"It is possible if you could identify a higher MMP profile you may want to stage them more urgently because their disease may progress more rapidly," he said. "With the early screening, we hope we can prevent people from getting to end-stage heart failure and reduce the number of people on the heart transplant list."

Spinale said that if cardiologists could slow the natural history of end stage heart failure by 10 years, we could reduce the cost of treating heart failure by 50 percent.

Source: Medical University of South Carolina