Researcher is first to identify cellular patterns of contraction in human hearts

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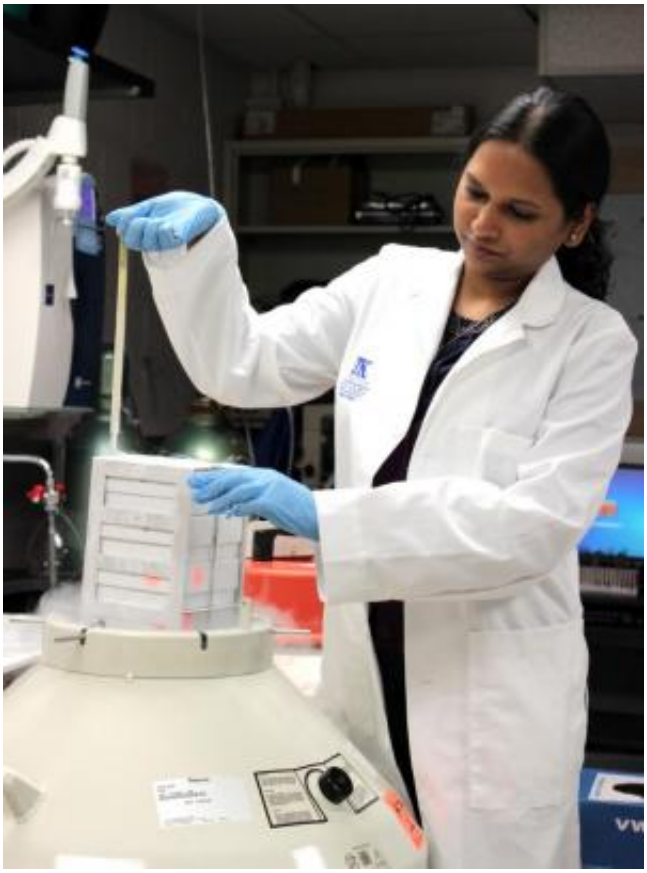

This is Premi Haynes. Credit: Roxane Poskin, University of Kentucky

When Premi Haynes was growing up in Pune, India, she attended Stella Maris High School, an English language convent school founded by Swiss nuns. Her second grade singing class used a book of English songs.

One of the songs was "My Old Kentucky Home." At that time, Haynes had never heard of Kentucky, had no idea where it was, and had no particular ambition to go there.

Some 20 years and a twist of fate later, on March 19 Haynes successfully defended her Ph.D. thesis in physiology at the University of Kentucky, where she's made a significant discovery about the cellular structure of the human heart, particularly related to heart failure. The findings have recently been published by the *Journal of Molecular and Cellular Cardiology*.

At 18, Haynes moved to the United States by herself. She had planned to go to college in her home country of India, but a family friend who had attended the University of the Cumberlands suggested that she apply there.

"It was serendipitous," she said. "Cumberlands was the only place I applied in the U.S., and I got a scholarship."

Then, the president of the university wrote her a letter encouraging her to come.

"It was hard to say no to that," she recalled. "And my parents said I could go, so I decided to try it. I had two suitcases and $200, which I thought was a lot of money."

Haynes has lived in Kentucky for the 12 years since then, completing her master's degree in biology at Morehead State University before enrolling in the Integrated Biomedical Sciences program at UK in 2008.

"I got interested in research when I was doing my master's at Morehead, and then I was interested in UK because it has an integrated program," she said. "I wasn't really sure which lab I wanted to go into, but at UK I

could do rotations and try different labs."

She ultimately decided to join the Campbell Muscle Lab under the mentorship of Ken Campbell, associate professor of physiology and director of the biospecimens core for the Center for Clinical and Translational Science (CCTS). When Haynes joined UK, Campbell had just started building a biobank of cardiac tissue. He only had a handful of samples at the time, but Haynes couldn't turn down the opportunity to study human tissue.

"I was really interested in translational research. I didn't want to work just on animal models, but also with human tissue," she said.

Haynes has been directly involved with the establishment and growth of the lab's biobank, which, five years later, now houses around 2,500 cardiac tissue samples from about 150 patients. The remarkable progress is the result of determined effort, institutional support, and collaboration to overcome the administrative and communication barriers of collecting cardiac tissue from patients with heart failure who are undergoing surgeries, and from organ donors.

"It's required an amazing commitment from the people in my lab," said Campbell.

To illustrate: Twenty-four hours a day, seven days a week, someone from the Campbell Muscle Lab is on call to rush to the operating room whenever there's a transplant or ventricular assist device (VAD) surgery from which they can collect a tissue sample.

"For five years, we haven't missed even one call," Haynes said. "And I think that's huge because the clinical staff know that we are invested in this, and we're determined to get these samples—they are very valuable. Groups in Washington state, Pennsylvania, and even New Zealand want

to collaborate with us so that they can use them."

And the hard work has paid off. Haynes' study is the first ever to document the specific cellular patterns of contraction across the wall of the human heart. As explained in her recent paper, "Transmural heterogeneity of cellular level power output is reduced in human heart failure," she showed that the different regions of the left ventricular wall have different cellular patterns of mechanical properties. Specifically, due to these transmural patterns, the middle of the wall is a better "engine" for pumping blood than the outer edges of the heart.

"People look at the heart as if the muscle is the same in every region of the heart. But that's not true," she said.

By comparing tissue from failing and non-failing hearts, she furthermore found that heart failure diminishes the cellular pattern (and therefore the pumping capacity) across the ventricular wall. Importantly, Haynes also discovered some of the key proteins that are driving these changes, which identifies new therapeutic targets for heart failure.

"Now we have some idea of which parts of the heart aren't working, and we can try to fix them to help treat disease," said Campbell.

Campbell and Haynes are quick to emphasize all of the different people and organizations at UK that have contributed to the success of their study. For example, the project was supported in part by a grant from the Center for Clinical and Translational Science. The Campbell Muscle Lab has also worked closely with the Center for Transplantation and Organ Failure, and in particular with Dr. Charles Hoopes, director of the UK Heart and Lung Transplant Program and the director of the Ventricular Assist Device (VAD) Program. In order to obtain samples of non-failing hearts, they've also worked with the Kentucky Organ Donor Affiliates team at UK. And they've depended significantly on the

circulating nurses in the operating room, who alert the on-call lab member whenever they might be able to obtain a tissue sample.

"Basic scientists are used to writing grants and doing experiments. And in the operating room, everybody is focused on keeping patients alive. It's a bit of a cultural change," said Campbell. "But our success will make it easier for the next group who try to do this type of translational work."

Haynes's project epitomizes the unique opportunities at UK to improve health by aligning advanced subspecialty care, such as transplants and VAD procedures, with basic science research. To further accelerate such progress, Campbell used support from the Center for Muscle Biology to start the Heart Working Group. Cardiologists, surgeons, and scientists now meet every Friday in the Department of Physiology to discuss their results and plan new research.

"We're not just doing operations—we're really making contributions to the field," Hoopes said.

Haynes is similarly aware of the value of this type of translational research.

"We've done a lot to cure heart failure in animals. But it's really time to cure heart failure in people," she said. "And I think that combining work on human and animal samples is the best way forward. We can learn things from humans, test our ideas with animals, and then go back to patients with potential therapies."

Haynes plans to build upon her findings through post-doctoral or industry work. While she admits that it might lead her to relocate, she knows that Kentucky will always be a home to her.

"I've been singing 'My Old Kentucky Home' for years," she said.

Provided by University of Kentucky