# Gene regenerates heart tissue, critical finding for heart failure prevention

April 17 2013

Researchers at UT Southwestern Medical Center have identified a specific gene that regulates the heart's ability to regenerate after injuries.

The function of the gene, called *Meis1*, in the heart was not known previously. The findings of the UTSW investigation are available online in *Nature*.

"We found that the activity of the *Meis1* gene increases significantly in heart cells soon after birth, right around the time heart muscle cells stop dividing. Based on this observation we asked a simple question: If the *Meis1* gene is deleted from the heart, will heart cells continue to divide through adulthood? The answer is 'yes'," said Dr. Hesham Sadek, assistant professor of internal medicine in the division of cardiology, and senior author of the study.

In 2011, Dr. Sadek's laboratory showed that the newborn mammalian heart is capable of a vigorous, regenerative response to injury through division of its own cells. As the newborn develops, the heart rapidly loses the ability to regenerate and to repair injuries such as heart attacks.

The research team demonstrated that deletion of *Meis1* extended the proliferation period in the hearts of newborn mice, and also re-activated the regenerative process in the adult mouse heart without harmful effect on cardiac functions. This new finding demonstrates that *Meis1* is a key factor in the regeneration process, and the understanding of the gene's

function may lead to new therapeutic options for adult heart regeneration. The findings also provide a possible alternative to current adult heart regeneration research, which focuses on the use of stem cells to replace damaged heart cells.

"*Meis1* is a transcription factor, which acts like a software program that has the ability to control the function of other genes. In this case, we found that Meis1 controls several genes that normally act as brakes on cell division," Dr. Sadek said. "As such, *Meis1* could possibly be used as an on/off switch for making adult heart cells divide. If done successfully, this ability could introduce a new era in treatment for heart failure."

According to the American Heart Association, almost 6 million people in the U.S. have heart failure, which occurs when the heart cannot pump enough blood and oxygen to support other organs. Heart disease is the leading cause of death for both men and women in the country, according to the Centers for Disease Control and Prevention.

The study received support from the American Heart Association, the Gilead Research Scholars Program in Cardiovascular Disease, the Foundation for Heart Failure Research, and the National Institutes of Health.

The co-first authors of the study are Dr. Ahmed I. Mahmoud, who is now a postdoctoral fellow at Harvard University; Dr. Fatih Kocabas, who is now a postdoctoral fellow at North American College; and Dr. Shalini A. Muralidhar, a postdoctoral research fellow II of internal medicine. Other researchers at UT Southwestern involved in the study are Wataru Kimura, a visiting senior researcher of internal medicine; Ahmed Koura, now a medical student at Ain Shams University in Egypt; Dr. Enzo Porrello, research fellow and faculty member at the University of Queensland in Australia; and Suwannee Thet, a research associate of internal medicine.

**More information:** Paper dx.doi.org/10.1038/nature12054