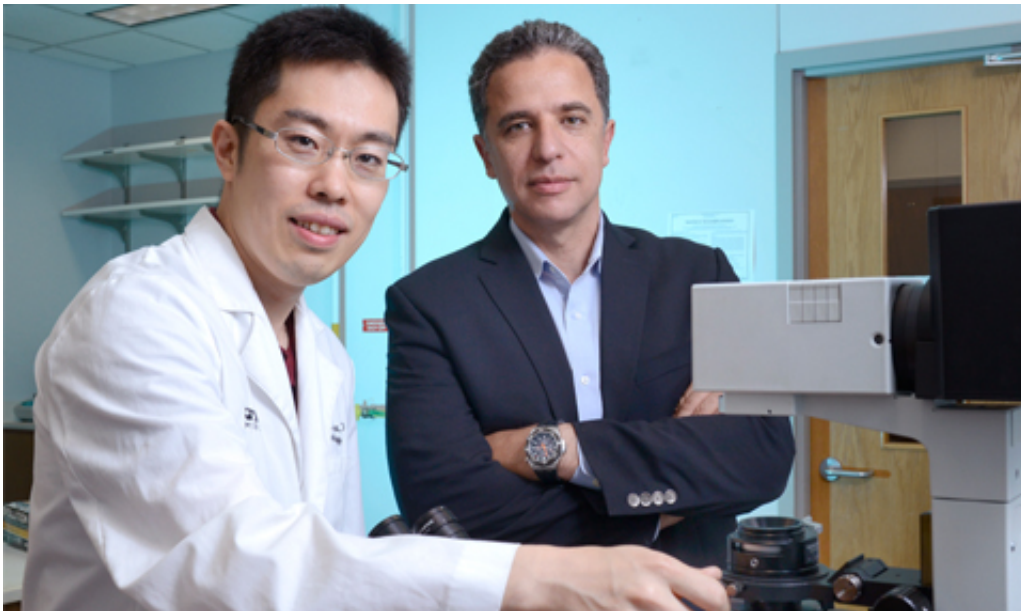


Researchers find cell that replenishes heart muscle

June 22 2015



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Regenerative medicine researchers at UT Southwestern Medical Center have identified a cell that replenishes adult heart muscle by using a new cell lineage-tracing technique they devised.

Adult heart muscle is comprised of [cells](#) called cardiomyocytes. Most cardiomyocytes don't replenish themselves after a [heart attack](#) or other

significant heart muscle damage. The UT Southwestern researchers were able to devise a new cell-tracing technique, allowing them to detect cells that do replenish themselves after being damaged.

"We identified a cell that generates new heart [muscle cells](#). This cell does not appear to be a stem cell, but rather a specialized cardiomyocyte, or heart muscle cell, that can divide, which the majority of cardiomyocytes cannot do," said Dr. Hesham Sadek, Assistant Professor of Internal Medicine and with the Hamon Center for Regenerative Science and Medicine.

Previous research by UT Southwestern scientists revealed that it is the highly oxygenated environment of the heart that prevents most [heart muscle cells](#) from dividing. The researchers reasoned that the cells that do divide must, therefore, be low on oxygen, which is a condition called hypoxic. They then devised a technique to identify and trace the lineage of hypoxic cells. That technique led them to the identification of the proliferating cells within heart muscle.

"For decades, researchers have been trying to find the specialized cells that make new muscle cells in the adult heart, and we think that we have found that cell," said Dr. Sadek, senior author of the study, which appears online in *Nature*.

"Now we have a target to study. If we can expand this cell population, or make it divide more, then we can make new muscle cells. This is what this cell does naturally, and we can now work toward harnessing this ability to make new heart muscle when the heart has been damaged."

The researchers found hypoxic microenvironments with proliferating cells scattered throughout the [heart muscle](#). They found the rate of formation of new cells to be between 0.3 percent and 1 percent annually.

"This is exciting work from both scientific and methodological standpoints," said Dr. Joseph Hill, Chief of the Division of Cardiology and Professor of Internal Medicine at UT Southwestern, who holds the James T. Willerson, M.D. Distinguished Chair in Cardiovascular Diseases and the Frank M. Ryburn, Jr. Chair in Heart Research. "Dr. Sadek's discovery points to a novel mechanism of cell-cycle control in cardiac myocytes and lends credence to the potential for regenerating - rebuilding - the diseased heart."

The new technique used to find the regenerative cells, a process called fate mapping, is an equally important development that may prove useful for distinguishing similar regenerating cells in other organs, as well as in cancers, the researchers said.

Traditional fate mapping, which is somewhat like developing a family tree for cells, labels cells based on the expression of a certain gene. That didn't work for the hypoxic cells, which are mainly regulated at the protein level rather than the gene-expression level. Instead, the researchers developed a sophisticated protein-tracking technique based on the presence of a hypoxia-responsive protein called Hif-1alpha. Researchers developed a genetically modified mouse in which the Hif-1alpha protein is fused to another protein, called Cre recombinase, which could then be used for cellular labeling.

"This fate-mapping approach, based on protein stabilization rather than gene expression, is an important tool for studying hypoxia in the whole organism. It can identify any hypoxic cell, not just cardiomyocytes, so this has broad implications for cellular turnover in any organ, and even in cancer," said Dr. Sadek, whose lab focuses on cardiac regeneration and stem cell metabolism.

More information: Hypoxia fate mapping identifies cycling cardiomyocytes in the adult heart, [DOI: 10.1038/nature14582](https://doi.org/10.1038/nature14582)

Provided by UT Southwestern Medical Center

Citation: Researchers find cell that replenishes heart muscle (2015, June 22) retrieved 6 May 2024 from <https://medicalxpress.com/news/2015-06-cell-replenishes-heart-muscle.html>

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