Fetal stem cells from placenta may help maternal heart recover from injury

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Researchers from Mount Sinai School of Medicine have discovered the therapeutic benefit of fetal stem cells in helping the maternal heart recover after heart attack or other injury. The research, which marks a significant advancement in cardiac regenerative medicine, was presented today at the American Heart Association's (AHA) Scientific Sessions 2011 in Orlando, Florida, and is also published in the current issue of *Circulation Research*, a journal of the AHA.

In the first study of its kind, the Mount Sinai researchers found that fetal stem cells from the placenta migrate to the heart of the mother and home to the site where an injury, such as a heart attack, occurred. The stem cells then reprogram themselves as beating heart stem cells to aid in its repair. The scientists also mimicked this reprogramming in vitro, showing that the fetal cells became spontaneously beating heart cells in cell culture, which has broad-reaching implications in treating heart disease.

Previous studies have documented a phenomenon in which half of women with a type of heart failure called peripartum cardiomyopathy saw their condition spontaneously recover in the months following pregnancy. Based on this evidence, the Mount Sinai team wanted to determine whether fetal stem cells played a role in maternal recovery.

They evaluated the hearts of pregnant female mice that underwent mid-gestation heart injury and survived. Using green fluorescent protein in the fetuses to tag the fetal stem cells derived from the placenta, they found that the green fluorescent stem cells homed to the injured hearts of their mothers, grafted onto the damaged tissue, and differentiated into smooth muscle cells, blood vessel cells, or another type of heart cell called cardiomyocytes.

"Our research shows that fetal stem cells play an important role in inducing maternal cardiac repair," said Hina Chaudhry, MD, Director of Cardiovascular Regenerative Medicine at Mount Sinai School of Medicine, and principal investigator of the study. "This is an exciting development that has far-reaching therapeutic potential."

With a broader understanding of the role of fetal stem cells, Dr. Chaudhry and her team then isolated the fetal cells that had grafted onto the maternal hearts and recreated the environment in vitro. They found that the cells spontaneously differentiated into cardiac cells in cell culture as well.

Until now, researchers have had limited success in discovering the regenerative potential of stem cells in heart disease. The use of bone marrow cells in cardiac regeneration has largely failed as well. Dr. Chaudhry's research team has found that fetal cells may potentially be a viable therapeutic agent, both through in vivo and in vitro studies.

"Identifying an ideal stem cell type for cardiac regeneration has been a major challenge in heart disease research," said Dr. Chaudhry. "Embryonic stem cells have shown potential but come with ethical concerns. We've shown that fetal stem cells derived from the placenta, which is discarded postpartum, have significant promise. This marks a significant step forward in cardiac regenerative medicine."

These findings have implications beyond cardiovascular disease. The fetal stem cells traveled only to the injury site on the damaged heart, and not to other undamaged organs, meaning research on the benefit of these cells on organs damaged by other diseases would be beneficial. Importantly, a significant percentage of the fetal cells isolated from maternal hearts express a protein called Cdx2, which indicates that the cells may not have developed mature immune recognition molecules and therefore are unlikely to cause a negative immune response, which occurs

in organ transplant.

"Our study shows the promise of these cells beyond just cardiovascular disease," said Dr. Chaudhry. "Additionally, this breakthrough greatly underscores the importance of translational research. As a clinician who also has a basic science laboratory, I am in the unique position to assess the needs of my patients, evaluate how they respond to treatment and recover from illness, and bring that anecdotal knowledge to the experiments in my lab."

Provided by The Mount Sinai Hospital