Amniotic fluid cells more efficiently reprogrammed to pluripotency than adult cells

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In a breakthrough that may help fill a critical need in stem cell research and patient care, researchers at Mount Sinai School of Medicine have demonstrated that skin cells found in human amniotic fluid can be efficiently "reprogrammed" to pluripotency, where they have characteristics similar to human embryonic stem cells that can develop into almost any type of cell in the human body. The study is online now and will appear in print in the next issue of the journal *Cellular Reprogramming*, to be published next month.

The Mount Sinai researchers found that when compared to cultured adult skin cells, the amniotic fluid skin cells formed stem cell colonies in about half the time and yielded nearly a 200 percent increase in number. Reprogramming fetal skin cells also cuts significantly the cost of generating patient-specific induced pluripotent stem cells when compared to reprogramming other cell types.

"There remains today a need in stem cell research for an easily reprogrammable cell type," said the study's lead author, Dr. Katalin Polgar, Assistant Professor of Medicine, Cardiology and Obstetrics, Gynecology and Reproductive Science, Mount Sinai School of Medicine. "Our study shows that reprogramming of cultured, terminally differentiated amniotic fluid cells results in pluripotent stem cells that are identical to human embryonic stem cells, and that it is much easier, faster and more efficient than reprogramming neonatal and adult cells."

Amniotic fluid skin cells can be safely obtained from pregnant women undergoing amniocentesis at about 15 weeks of pregnancy as part of a diagnostic workup for chromosome aberrations and other genetic diseases. About 99 percent of cells found in amniotic fluid are terminally differentiated cells mostly from fetal skin, which are shed into the amniotic fluid as a fetus develops. Since these cells can be reprogrammed to pluripotency more efficiently than other cell types, they could be an important source for generating stem cells for basic research and future therapies and may be used to study and potentially cure fatal embryonic diseases with prenatal, perinatal gene therapy.

"We induced amniotic fluid skin cells to return from their final differentiated stage back to an undifferentiated stem cell stage from where they can develop into any cell type of the body," said Dr. Polgar. "

Amniotic fluid cells work much better than any other cell types when turning back their 'internal clock.' These cells can potentially be used as a model system in studying different regenerative therapies for diseases of the heart, liver, kidney, lung, pancreas, as well as for replacement of lost neurons in Alzheimer's, Parkinson's, even for cancer vaccines. They may also be used for future personalized stem cell banks. As the pluripotent stem cells induced from amniotic fluid skin cells are the patient's own cells, there is no risk of immunorejection or teratocarcinoma formation.

"Additionally, stem cells reprogrammed from amniotic fluid skin cells could be used for drug discovery in disease models," added Dr. Polgar. "Their potential use in toxicology models could reduce the need for experimental animals. Developing cell lines from individual amniotic fluid samples can accelerate the development of existing targets for different diseases. This all will bring new opportunities to explore innovative therapeutic models or targets in regenerative personalized medicine."

The scientists were able to genetically reprogram the amniotic fluid skin cells using the four transcription factors (proteins that regulate the transcription of genes) OCT3/4, SOX2, KLF4, and c-MYC. After reprogramming, the cells were found to be identical to human embryonic stem cells in numerous ways, including for morphological and growth characteristics, antigenic stem cell markers, stem cell gene expression, and telomerase activity, in vitro and in vivo differentiation.

"These reprogrammed amniotic fluid cells are able to form, as embryonic stem cells can, three dimensional spheroid structures called 'embryoid bodies.' They also have the ability to self-renew themselves indefinitely. Pluripotent stem cells created from amniotic fluid cells shed from the fetal skin maintain all the potential of embryonic stem cells without using embryos, thereby eliminating ethical concerns associated with human embryonic stem cells obtained from preimplantation embryos," Dr. Polgar said.

Provided by Mount Sinai School of Medicine