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Amniotic fluid may provide new source of stem cells for future therapies

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For the first time, scientists have shown that amniotic fluid (the protective liquid surrounding an embryo) may be a potential new source of stem cells for therapeutic applications. The study was prepublished online on February 12, 2009, in *Blood*, the official journal of the American Society of Hematology.

"Building on observations made by other scientists, our research team wondered whether stem cells could be detected in amniotic fluid. We looked at the capacity of these cells to form new blood cells both inside and outside the body, and also compared their characteristics to other well-known sources of stem cells," said senior study author Marina Cavazzana-Calvo, MD, PhD, of INSERM, the national French institute for health and biomedical research. Isabelle André-Schmutz, PhD, of INSERM, also a senior author of the study, added, "The answer was a resounding 'yes' - the cells we isolated from the amniotic fluid are a new source of stem cells that may potentially be used to treat a variety of human diseases."

To conduct the study, amniotic fluid was collected from pregnant mice between 9.5 and 19.5 days post-coitus. Human amniotic fluid was collected during routine diagnostic procedures (amniocentesis) from volunteer donors between seven and 35 weeks of pregnancy.

Amniotic fluid (AF) cells that had markers similar to bone marrow stem cells (termed AFKL cells) were then isolated for use in experiments, as these cell markers were indicative of progenitor cells (cells that have the

capacity to differentiate into other types of cells).

In vitro, AFKL cells from both mice and humans were able to generate all blood cell lineages, including red (erythroid) blood cells and white (myeloid and lymphoid) blood cells in experiments performed outside the animals. But the scientists also wanted to explore the AFKL cells' hematopoietic (blood-forming) potential in vivo. Therefore, adult mice were irradiated to destroy their capacity to produce blood cells and injected with either AFKL cells or fetal liver cells. Fetal liver was used for comparison as it is the primary source for hematopoietic cells in developing embryos.

The peripheral blood of the transplanted mice was examined every four weeks, and after 16-18 weeks the blood-forming organs (bone marrow, spleen, thymus, and lymph nodes) of the mice were dissected. Transplants using mouse AFKL cells were found to be successful; newly formed white blood cells of all lineages derived from AFKL cells appeared in most of the irradiated mice four weeks after the procedure. As expected, all of these blood cell types were detected in all of the control group mice who received fetal liver cell transplants. Scientists continued to find AFKL-derived cells in the irradiated mice four months later, demonstrating the long-term ability of the transplanted cells to produce new blood cells.

Bone marrow samples from the transplanted mice were also taken and injected in a second set of mice and the peripheral blood of this new group of irradiated mice was analyzed and their hematopoietic organs examined after 10-13 weeks. The secondary transplants with mouse AFKL cells were partially successful with some of the mice engrafting the donor cells. This finding shows that AFKL cells have the ability to self-renew, a key characteristic of stem cells.

Though the human AFKL cells failed to reconstitute the hematopoietic

system in irradiated, immunodeficient mice, experiments are currently underway to overcome obstacles that may have led to this failure, such as using a low number of cells for the injection and conducting the transplant in adult mice (engraftment is easier to obtain in newborn mice).

As additional confirmation of the probability that AFKL cells are indeed stem cells, the researchers examined them for the expression of specific genes known to be involved in hematopoietic development. The overall gene expression profile of the AFKL cells was found to resemble blood cell progenitors from known hematopoiesis sites such as the aorta-gonadmesonephros region, placenta, and the umbilical/vitelline arteries.

Source: American Society of Hematology

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