Reprogrammed human blood cells show promise for disease research

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Cells from frozen human blood samples can be reprogrammed to an embryonic-stem-cell-like state, according to Whitehead Institute researchers. These cells can be multiplied and used to study the genetic and molecular mechanisms of blood disorders and other diseases.

The research is reported in the July 2 issue of *Cell Stem Cell*.

To date, most cellular reprogramming has relied on skin biopsy or the use of stimulating factors to obtain the cells for induction of pluripotency. This work shows for the first time that cells from blood samples commonly drawn in doctor's offices and hospitals can be used to create induced pluripotent stem (iPS) cells.

Using blood as a cell source of iPS cells has two major advantages.

"Blood is the easiest, most accessible source of cells, because you'd rather have 20 milliliters of blood drawn than have a punch biopsy taken to get skin cells," says Judith Staerk, first author of the Cell Stem Cell paper and a postdoctoral researcher in the lab of Whitehead Founding Member Rudolf Jaenisch.

Also, blood collection and storage is a well established part of the medical system.

"There are enormous resources—blood banks with samples from patients—that may hold the only viable cells from patients who may not

be alive anymore or from the early stage of their diseases," says Jaenisch, who is also a professor of biology at MIT. "Using this method, we can now resurrect those cells as induced pluripotent stem cells. If the patient had a neurodegenerative disease, you can use the iPS cells to study that disease."

iPS cells are reprogrammed from an adult state to an embryonic stem-cell-like state by inserting four reprogramming genes into the adult cells' DNA. These reprogramming factors convert the adult cells, with defined cell functions, into much more flexible iPS cells. iPS cells can then be nudged to divide repeatedly or turn into almost any cell type found in the body, allowing scientists to create large amounts of the specific cells needed to study a disease, such as dopamine-producing neurons for Parkinson's disease research.

Unlike other cell types, human blood cells had proven extremely difficult to convert into iPS cells. Working with frozen blood samples similar to those found in a blood bank, Staerk found that she could convert the blood cells by inserting a "cassette" of the reprogramming factors end to end, rather than inserting each of the factors separately.

Not all of the cells in the blood samples were converted to iPS cells. Blood is composed of red cells that carry oxygen throughout the body, white cells that are part of the immune system, and platelets that clot the blood after an injury. Because red blood cells and platelets lack nuclei containing DNA, they cannot be converted to iPS cells. The only white bloods cells converted to iPS cells were T cells and a few myeloid cells. B cells failed to reprogram, most likely because the experiment's environment lacked the chemicals needed for successful B-cell conversion.

Staerk is particularly interested in using these iPS cells to study blood diseases.

"With this method, you could reprogram blood samples from patients where the underlying cause of their diseases is not known, and get cell numbers large enough to screen for genetic factors and study the molecular mechanisms underlying the blood disorders," she says. "That's a big advance, especially if the patient is not alive anymore and new material cannot be obtained."

More information: "Reprogramming of human peripheral blood cells to induced pluripotent stem cells", Cell Stem Cell, July 2, 2010.

Provided by Whitehead Institute for Biomedical Research