Scientists reprogram human skin cells into embryonic stem cells

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UCLA stem cell scientists have reprogrammed human skin cells into cells with the same unlimited properties as embryonic stem cells without using embryos or eggs.

Led by scientists Kathrin Plath and William Lowry, UCLA researchers used genetic alteration to turn back the clock on human skin cells and create cells that are nearly identical to human embryonic stem cells, which have the ability to become every cell type found in the human body. Four regulator genes were used to create the cells, called induced pluripotent stem cells or iPS cells.

The UCLA study confirms the work first reported in late November of researcher Shinya Yamanaka at Kyoto University and James Thompson at the University of Wisconsin. The UCLA research appears Feb. 11, 2008, in an early online edition of the journal *Proceedings of the National Academy of the Sciences*.

The implications for disease treatment could be significant. Reprogramming adult stem cells into embryonic stem cells could generate a potentially limitless source of immune-compatible cells for tissue engineering and transplantation medicine. A patient's skin cells, for example, could be reprogrammed into embryonic stem cells. Those embryonic stem cells could then be prodded into becoming various cells types – beta islet cells to treat diabetes, hematopoetic cells to create a new blood supply for a leukemia patient, motor neuron cells to treat Parkinson's disease.

“Our reprogrammed human skin cells were virtually indistinguishable from human embryonic stem cells,” said Plath, an assistant professor of biological chemistry, a researcher with the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research and lead author of the study. “Our findings are an important step towards manipulating differentiated human cells to generate an unlimited supply of patient specific pluripotent stem cells. We are very excited about the potential implications.”

The UCLA work was completed at about the same time the Yamanaka and Thomson reports were published. Taken together, the studies demonstrate that human iPS cells can be easily created by different laboratories and are likely to mark a milestone in stem cell-based regenerative medicine, Plath said.

These new techniques to develop stem cells could potentially replace a controversial method used to reprogram cells, somatic cell nuclear transfer (SCNT), sometimes referred to as therapeutic cloning. To date, therapeutic cloning has not been successful in humans. However, top stem cell scientists worldwide stress that further research comparing these reprogrammed cells with stem cells derived from embryos, considered the gold standard, is necessary. Additionally, many technical problems, such as the use of viruses to deliver the four genes for reprogramming, need to be overcome to produce safe iPS cells that can be used in the clinic.

“Reprogramming normal human cells into cells with identical properties to those in embryonic stem cells without SCNT may have important therapeutic ramifications and provide us with another valuable method to develop human stem cell lines,” said Lowry, an assistant professor of molecular, cell and developmental biology, a Broad Stem Cell Center researcher and first author of the study. “It is important to remember that our research does not eliminate the need for embryo-based human

embryonic stem cell research, but rather provides another avenue of worthwhile investigation."

The combination of four genes used to reprogram the skin cells regulate expression of downstream genes and either activate or silence their expression. The reprogrammed cells were not just functionally identical to embryonic stem cells. They also had identical biological structure, expressed the same genes and could be coaxed into giving rise to the same cell types as human embryonic stem cells.

The UCLA research team included four young scientists recruited to UCLA's new stem cell center in the wake of the passage of Proposition 71 in 2004, which created $3 billion in funding for embryonic stem cell research. The scientists were drawn to UCLA in part because of California's stem cell research friendly atmosphere and the funding opportunities created by Proposition 71. In addition to Plath and Lowry, the team included Amander Clarke, an assistant professor of molecular, cell and developmental biology, and April Pyle, an assistant professor of microbiology, immunology and molecular genetics.

The creation of the human iPS cells is an extension of Plath's work on mouse stem cell reprogramming. Plath headed up one of three research teams that were able to successfully reprogram mouse skin cells into mouse embryonic stem cells. That work appeared in the inaugural June 2007 issue of the journal *Cell Stem Cell*.

Source: University of California - Los Angeles