Scientists develop method for generating novel types of stem cells

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The study, which appears in the December 18 online version of *Cell Stem Cell* and the January 2009 print edition of the journal, provides proof of principle that alternative sources of stem cells can be created.

The team, which included scientists from Scripps Research, Peking University, and the University of California, San Diego, conducted the studies to establish novel rat induced pluripotent stem cell lines (riPSCs) and human induced pluripotent stem cell lines (hiPSCs) by using a specific cocktail of chemicals combined with genetic reprogramming, a process whereby an adult cell is returned to its early embryonic state. Pluripotency refers to the ability of a cell to develop into each of the more than 200 cell types of the adult body.

Mimicking Human Physiology

The major advantage of using other animal species, such as rats, is that the physiology of these animals can better mimic human physiology, for example, in studies of metabolic and neurological diseases. The size of other animals also is an advantage because larger organs and tissues are easier to work with. Because of these benefits, scientists have created transgenic animals from species other than mice, but the lack of pluripotent stem cells from these species and the tedious and imprecise techniques currently available has made the process difficult.

"Mouse models created with pluripotent embryonic stem cells are

wonderful tools for understanding the fundamental biology of genes," says Sheng Ding, Ph.D., an associate professor in the Scripps Research Department of Chemistry who was senior author of the study with Peking University investigator Hongkui Deng, Ph.D. "But in some important ways these models are less than ideal. Our demonstrated technologies will enable unprecedented and broad applications for better creating animal models from other species."

Novel and More Robust Human Pluripotent Stem Cells

"Recent studies have found, however, that conventional human embryonic stem cells represent a different pluripotent cell type and are not the counterpart of the conventional, and most useful, mouse embryonic stem cells," Ding says.

The issue is that pluripotent stem cells can be represented by cells from two distinct stages of embryonic development—the early pre-implantation blastocyst stage and the later post-implantation epiblast stage. Today, conventional mouse embryonic stem cells represent the pre- implantation stage pluripotent cells, and human embryonic stem cells appear to represent later post- implantation stage pluripotent cells.

Early- and late-stage cells have very different properties. For example, they respond differently to the same signals given to stem cells to differentiate into specific types of cells. The pre-implantation stage of cells will differentiate into one type of cell, while post-implantation stage of cells will turn into other types of cells. Their propensity toward specific cell types and growth properties are also different. The novel human pluripotent cells created by the scientists appear to represent the early stage of pluripotent cells—closer to well researched conventional mouse embryonic stem cells—and grow with better properties.

"The different behaviors of the pre- and post-implantation pluripotent stem cells means that findings from research done on mouse embryonic stem cells are often not translatable to work done on human embryonic stem cells," Ding says. "With our new human pluripotent stem cells, we again have proof of principle that human stem cells can be created that are similar to mouse embryonic stem cells. The knowledge gained from mouse studies, therefore, will be more directly translatable to human cells, offering an advantage in biomedical research."

Source: Scripps Research Institute