Critical similarity between two types of do-it-all stem cells revealed in new study

September 11 2011, by David Tenenbaum

Ever since human induced pluripotent stem cells were first derived in 2007, scientists have wondered whether they were functionally equivalent to embryonic stem cells, which are sourced in early-stage embryos.

Both cell types have the ability to differentiate into any cell in the body, but their origins – in embryonic and adult tissue – suggest that they are not identical.

Although both cell types have great potential in basic biological research and in cell- and tissue-replacement therapy, the newer form, called IPS cells, have two advantages. They face less ethical constraint, as they do not require embryos. And they could be more useful in cell replacement therapies: growing them from the patient's own cells would avoid immune rejection.

But until IPS cells are proven to have the same traits as embryonic stem cells, they cannot be considered to be identical.

In a study published today (Sunday, Sept. 11), researchers at the University of Wisconsin-Madison report the first full measurement of the proteins made by both types of stem cells. In a study that looked at four embryonic stem cells and four IPS cells, the proteins turned out to be 99 percent similar, says Joshua Coon, an associate professor of chemistry and biomolecular chemistry who directed the project.

"We looked at RNA, at proteins, and at structures on the proteins that help regulate their activity, and saw substantial similarity between the two stem-cell types," he says.

Proteins are complex molecules made by cells for innumerable structural and chemical purposes, and the new study measured more than 6,000 individual proteins using highly accurate mass spectrometry, a technique that measures mass as the first step of identifying proteins.

The study in *Nature Methods*, published online, is the first comprehensive comparison of proteins in the two stem cell types, says Doug Phanstiel, who is now at Stanford University, and worked with Justin Brumbaugh on the project as graduate students at UW-Madison.

"From a biological standpoint, what is novel is that this is the first proteomic comparison of embryonic stem cells and IPS cells," says Phanstiel, referring to the study of which proteins a cell produces.

In essence, every cell in the body has the genes to make any protein the body might need, but cells make only the proteins that further their own biological role. Cells regulate the formation and activity of proteins in three ways: first, by controlling the production of RNA, a molecule that transfers the DNA code to protein-making structures; second, by controlling the quantity of each protein made; and third, by adding structures to the protein that regulate when it will be active.

The new study measured each of these activities, Phanstiel says.

"And because we compared four lines of each type of stem cell, and the comparisons were run three times, the statistics are extremely robust," he adds.

The new report, Coon says, suggests that embryonic stem cells and IPS

cells are quite similar. According to some measurements, the protein production of an embryonic stem cell was closer to that of an IPS cell than to a second embryonic stem cell.

The ability to measure proteins in such detail emerged from improved ways to measure mass, Coon says.

"New technical developments in both our ability to measure a protein's mass – accurate to the third or fourth decimal place – and to compare the proteins from up to eight different cell lines at a time -- permitted this important comparison for the first time," says Coon.

The study is not the last word in determining the similarity of the two types of pluripotent stem cells, says Coon, who worked with UW-Madison stem-cell pioneer James Thomson, on the project.

Because clinical uses of either type of stem cells will require that they be transformed into more specialized cells, researchers still need to know more about protein production after a stem cell is differentiated into, for example, a neuron or heart muscle cell.

This technology, Coon says, "is now well-positioned to study how closely molecules contained in these promising cells change after they are differentiated into the cells that do the work in our bodies – a critical next step in regenerative medicine."

Provided by University of Wisconsin-Madison