Induced neural stem cells: Not quite ready for prime time

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(PhysOrg.com) -- The great promise of induced pluripotent stem cells is that the all-purpose cells seem capable of performing all the same tricks as embryonic stem cells, but without the controversy.

However, a new study published this week (Feb. 15) in the Proceedings of the National Academy of Sciences comparing the ability of induced cells and embryonic cells to morph into the cells of the brain has found that induced cells — even those free of the genetic factors used to program their all-purpose qualities — differentiate less efficiently and faithfully than their embryonic counterparts.

The finding that induced cells are less predictable means there are more kinks to work out before they can be used reliably in a clinical setting, says Su-Chun Zhang, the senior author of the new study and a professor in the University of Wisconsin-Madison School of Medicine and Public Health.

"Embryonic stem cells can pretty much be predicted," says Zhang. "Induced cells cannot. That means that at this point there is still some work to be done to generate ideal induced pluripotent stem cells for application."

Scientists in the burgeoning field of regenerative medicine are pinning their hopes on induced stem cells because they offer advantages over embryonic stem cells, not the least of which is the fact that they do not need to be derived from early-stage human embryos.

The new Wisconsin study compared the ability of five embryonic stem cell lines with 12 induced cell lines coaxed into being using different methods. Embryonic stem cells are considered the "gold standard" for all pluripotent stem cells, which are cells that can differentiate into all of the 220 cell types in the human body.

Zhang's group, led by researcher Baoyang Hu, found that the induced cells differentiate into progenitor neural cells and further into the different kinds of functional neurons that make up the brain. However, that they do not faithfully mirror all the differentiation capabilities of embryonic cells suggests that there are unknown factors at play that may limit their use in terms of modeling disease in the laboratory, one of the most important potential early applications of stem cell technology. Such unknowns would also limit their use in clinical settings for such things as cell transplants.

Intriguingly, the new study suggests the presence or absence of the genes used to reprogram skin cells to become the blank slate pluripotent cells makes no difference in terms of their capacity to differentiate. Some of the induced stem cell lines tested in the study were made using techniques that bypassed the use of genes that had been used to reprogram skin cells to become pluripotent stem cells.

It was predicted, Zhang explains, that the absence of exotic genetic factors would result in cells essentially identical to embryonic stem cells. "It is totally surprising that doesn't happen at all," says Zhang. "It tells us the techniques for generating induced pluripotent stem cells are still not optimal. There is room for improvement."

Despite their unpredictability, Zhang notes that induced stem cells can still be used to make pure populations of specific types of cells, making them useful for some applications such as testing potential new drugs for efficacy and toxicity. He also noted that the limitations identified by his

group are technical issues likely to be resolved relatively quickly.

"It appears to be a technical issue," he says. "Technical things can usually be overcome."

The key, he explains, is determining what things are at play that make the induced cells different.

Provided by University of Wisconsin-Madison