Inducing stem cells to become different cell types efficiently now possible using a three-dimensional platform

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Induced pluripotent stem (iPS) cells have the potential to form any cell type in the body, providing a powerful tool for drug discovery and regenerative medicine. Yet coaxing these cells to reliably take on a specific fate in the laboratory has proven challenging on a large scale. Now, a team of A*STAR stem cell researchers has developed a cell differentiation protocol in which iPS cells are propagated and expanded in a three-dimensional (3D) bioreactor to efficiently create neural progenitor cells.

"Such a method will be a boon for the nascent cell-therapy and drug-screening industry, as it will be able to produce vast amounts of cells for transplantation and drug discovery in a reproducible manner," says Steve Oh at the A*STAR Bioprocessing Technology Institute in Singapore, who led the research.

Oh and his co-workers started with a so-called 'microcarrier' platform that they had previously developed for culturing human embryonic stem cells on the surface of small solid particles in a 3D suspension system. They optimized the technology for human iPS cells, demonstrating that protein-coated cylindrical microcarriers in stirred vessels, known as spinner flasks, coupled with twice-daily culture medium exchange, can support 20-fold expansion of reprogrammed stem cells. This yield was higher than any other reported system for growing batches of such cells.

Normally, iPS cells would then have to be painstakingly manipulated on a flat Petri plate to form more specialized cells. But, with just a simple change of the growth medium in the new 3D set-up, the researchers induced the cells to become neural precursors with up to 85% efficiency. This integrated process of cell expansion and differentiation produced 333 neural progenitor cells for each iPS cell seeded. By comparison, the classic 2D tissue culture protocol, used by most scientists, gave rise to just 53 neural precursors per initial stem cell.

"The 2D approach is manually laborious, gives one-tenth of the yields and is variable from lab to lab," says Oh. "Microcarrier-based cultures provide larger surface areas for cell growth and more of them can be added to the system to increase the aggregate sizes and yields."

Oh and his team also coaxed the neural progenitors to further differentiate into many different types of brain cells, including neurons, oligodendrocytes and astrocytes—the three primary neural lineages. In the future, notes Oh, such neurons could be used to treat Parkinson's disease, for example; and, oligodendrocytes could be transplanted to overcome spinal cord injuries.

More information: Bardy, J., Chen, A. K., Lim, Y. M., Wu, S., Wei, S. et al. Microcarrier suspension cultures for high-density expansion and differentiation of human pluripotent stem cells to neural progenitor cells. *Tissue Engineering Part C: Methods* advance online publication, 4 September 2012 (doi: 10.1089/ten.tec.2012.0146). online.liebertpub.com/doi/abs/ … 89/ten.tec.2012.0146

Chen, A. K.-L., Chen, X., Choo, A. B. H., Reuveny, S. & Oh, S. K. W. Critical microcarrier properties affecting the expansion of undifferentiated human embryonic stem cells. *Stem Cell Research* 7, 97–111 (2011). www.sciencedirect.com/science/ … ii/S1873506111000614