Polymer boosts production of stem cells in three dimensions

Kyoto, Japan— Mass producing human pluripotent stem cells (hPSCs), including embryonic stem cells and induced pluripotent stem cells, for regenerative medicine and drug discovery may have gotten much easier, thanks to a polymer-based 3D culture system developed by Japanese researchers.

Their findings, published in the journal *Stem Cell Reports*, could one day be adopted for industrial scale manufacturing of hPSCs to meet the growing demand of large-scale and quality-controlled cells for drug discovery and cell-based therapy for patients.

Regenerative medicine is an emerging research field that uses healthy hPSC-based functional cells to replace diseased cells found in human illnesses such as Parkinson's disease and macular dystrophy. However, producing quality hPSCs in large quantities is complex and is expected to be a bottleneck in providing adequate supplies of cells for treatment purposes in the future.

"Typically hPSCs are grown in two dimensions while attached to a flat surface on a petri dish, which physically limits the amount we can grow and harvest at one time," explained Tomomi G. Otsuji, an author involved in the study.

The researchers — from Kyoto University's Institute for Integrated Cell-Materials Sciences (iCeMS) and **Nissan Chemical Industries, LTD** — grew stem cells in spherical aggregates, or clumps, and suspended them in three dimensions in a nutrient broth with the help of polymers that prevented spheres from sinking to the bottom.

"Our polymer-based 3D culture system provided similar cellular growth rates to those found in conventional 2D systems," said Kouichi Hasegawa, another researcher involved in the study. "Moreover, because we avoided pitfalls that are typically associated with other 3D culturing methods, such as spontaneous fusion of cell aggregates and premature differentiation, the hPSCs we grew were healthy and more than 95% of them retained their pluripotency even after several months of continuous growth in the 3D culture."

The researchers also showed that their system could be up-scaled for larger yields. As a proof of concept, they grew more than 100 million hPSCs in a single plastic bag with their 3D system, which would normally take anywhere from 10 to 20 large petri dishes to produce the same amount. These findings could lead to time and money savings on labor and resources involved in hPSC expansion.

"Our approach provides an excellent starting point for the large-scale production of hPSCs and ensures a homogenous source of high quality cells for therapeutic and drug discovery applications," said iCeMS Founding Director Norio Nakatsuji, who was the principal investigator of the study.