Scientists develop new protocol to ready induced pluripotent stem cell clinical application

April 3 2013

A team of New York Stem Cell Foundation (NYSCF) Research Institute scientists led by David Kahler, PhD, NYSCF Director of Laboratory Automation, have developed a new way to generate induced pluripotent stem (iPS) cell lines from human fibroblasts, acquired from both healthy and diseased donors. Reported in *PLOS ONE*, this cell-sorting method consistently selects the highest quality, standardized iPS cells, representing a major step forward for drug discovery and the development of cell therapies.

Employing a breakthrough method developed by 2012 Nobel laureate Shinya Yamanaka, MD, PhD, adult cells are "reprogrammed" or reverted to an embryonic-like state, commonly through viral infection. Reprogramming is a dynamic process, resulting in a mixture of fully reprogrammed iPS cells, partially reprogrammed cells, and residual adult cells. Previous protocols to select promising fully reprogrammed cells rely primarily on judging stem cell colonies by eye through a microscope .

Cell colonies selected by qualitative measures could include partially reprogrammed cells, a major concern for clinical applications of cell therapies because these cells could become any other cell type in a patient following transplantation. Additionally for drug efficacy assays and toxicity investigations on iPS cells, heterogeneous cell populations can mar the response of representative iPS cell lines.

The NYSCF scientists developed a quantitative protocol, optimized over three and a half years, in order to consistently harvest early-reprogrammed cells. Using fluorescence activated cell sorting (FACS), fully reprogrammed cells were identified by two specific proteins, or pluripotency markers. The group then looked at third marker that is expressed by partially reprogrammed or adult cells, and they then negatively selected against these cells to obtain only fully reprogrammed cells.

"To date, this protocol has enabled our group to derive (and characterize over) 228 individual iPS cell lines, representing one of the largest collections derived in a single lab," said Dr. Kahler. "This standardized method means that these iPS cells can be compared to one another, an essential step for the use in drug screens and the development of cell therapies."

This process of selecting stem cell colonies provides the basis for a new technology developed by NYSCF, The NYSCF Global Stem Cell Array (Array), a fully automated, robotic platform to generate cell lines in parallel. Currently underway at the NYSCF Laboratory, the Array reprograms thousands of healthy donors' and diseased patients' skin and/or blood samples into iPS cell lines. Sorting and characterizing cells at an early stage of reprogramming allows efficient development of iPS cell clones and derivation of adult cell types.

"We are enthusiastic about the promise this protocol holds to the field. As stem cells move towards the clinic, Dr. Kahler's work is a critical step to ensure safe, effective treatments for everyone," said Susan L. Solomon, CEO of NYSCF.

Provided by New York Stem Cell Foundation