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Guiding cells to improve life

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Fate Therapeutics Announces Creation of Small Molecule Platform for Commercial Scale Reprogramming

Development of Two Week Method for Generating Human Induced Pluripotent Stem Cells with 200-Fold Increase in Yield

La Jolla, CA – Fate Therapeutics, Inc. announced today the generation of human induced pluripotent stem cells (iPSCs) using a combination of small molecules that significantly improves the speed and efficiency of reprogramming. The discoveries, which were made by Sheng Ding, Ph.D., under a research collaboration between Fate Therapeutics and The Scripps Research Institute (TSRI), represent a more than 200 fold improvement in reprogramming efficiency and reduce the reprogramming period to two weeks as compared to methods using only the four reprogramming factors (Oct 3/4, Sox2, Klf4 and c-Myc). This latest advancement has broad implications for the creation of "pharmaceutical grade" iPSCs, reprogrammed cells that can be produced without genetic modification at commercial scale quantity, quality and consistency and continues to bolster the leadership position of Fate Therapeutics in industrialized iPSC technology. The Company is developing minimally invasive techniques for reprogramming and differentiation and has exclusively in-licensed from TSRI and the Whitehead Institute for Biomedical Research an intellectual property portfolio related to iPSC technology dating back to November 2003.

"While recent studies have reported improved methods of reprogramming, those techniques have relied on further genetic manipulation or have not otherwise addressed a fundamental reprogramming challenge – that iPSC generation is still a very slow and inefficient process and results in a heterogeneous population of cells," said Paul Grayson, president and CEO of Fate Therapeutics. "Once again, Dr. Ding and his team are the first group to clear yet another major hurdle required for the widespread commercial use of iPSCs for drug discovery and patient therapies."

The findings of Dr. Ding and his colleagues are published today in the Advanced Online edition of the scientific journal Nature Methods. As compared to using the four reprogramming factors of Oct 3/4, Sox2, Klf4 and c-Myc alone, Dr. Ding discovered a combined chemical approach that dramatically improves (> 200 fold) the generation of iPSCs from human fibroblasts within two weeks of retroviral transduction. The iPSC colonies generated by the Ding team using a three compound cocktail could be stably expanded over the long term (20+ passages), closely resembled human embryonic stem cells in terms of morphology and pluripotency marker expression and could be differentiated into derivatives of all the three germ layers both in vitro and in vivo.

"Once we achieved reprogramming with cell penetrating proteins, we targeted certain biological pathways that might improve speed and efficiency so as to enable the commercial scale production of patient-specific iPSCs for medical use," said Dr. Ding, associate professor of TSRI and scientific founder of Fate Therapeutics. "When combined with non-viral, non-DNA based methods for iPSC generation, we believe these discoveries create a powerful platform for safer, more efficient reprogramming of human somatic cells."

Earlier this year, under a research collaboration with Fate Therapeutics and TSRI, Dr. Ding and his team of scientists became the first group to generate iPSCs using non-viral, non-DNA based reprogramming methods. Instead of inserting the reprogramming factors of Oct 3/4, Sox2, Klf4 and c-Myc with DNA-based methods, such as viruses or plasmids, the scientists engineered and used recombinant proteins to reprogram cells without genetic modifications. The scientists found that those reprogrammed embryonic-like cells – dubbed "protein induced pluripotent stem cells" or "piPSCs" – from fibroblasts behave indistinguishably from classic embryonic stem cells in their molecular and functional features, including differentiation into various cell types, such as beating cardiac muscle cells, neurons, and pancreatic cells.