MedicalXpress

# Application of human induced pluripotent stem cells in precision medicine for hereditary diseases

May 8 2018

Researchers at Li Ka Shing Faculty of Medicine of The University of Hong Kong (HKU) have successfully demonstrated the use of human induced pluripotent stem cells (hiPSCs) from patients' skin cells for therapeutic drug testing. The success of the research implies that scientists are one step closer to applying stem cells in precision medicine in treating patients suffering from rare hereditary diseases.

Since its invention by two independent research teams led by Professor Shinya Yamanaka at Kyoto University, Japan and Professor James Thomson at University of Wisconsin-Madison in 2007, patient-specific iPSCs are an emerging approach to disease treatment and prevention that takes into account individual patient variability in environment, lifestyle, and genetic makeup. With the same genetic composition of the donor patients, and with the capacity to transform into all types of body cells, hiPSCs have emerged as the most promising candidate cell source for drug testing and drug screening.

The team has been working for years to develop hiPSC-based therapy for human diseases since 2008. In 2010, the team developed a custom-made protocol to generate animal product-free hiPSC. In the current study, hiPSC was generated from patients with a rare form hereditary cardiomyopathy due to mutations in the Lamin A/C (LMNA)-related cardiomyopathy in three families. Affected individuals suffer heart failure, stroke and sudden death at a relatively young age. To date, there

is no specific treatment for this condition.

The team tested a drug, PTC124, which can suppress certain genetic mutations in other hereditary disease in the patient-specific iPSC transformed heart muscle cells. In brief, the procedure could be explained as follows:

First, it was shown that these heart muscle cells reproduced the pathophysiological hallmarks of LMNA-related cardiomyopathy in a disc. Interestingly, PTC124 treatment restored gene function and reversed pathological processes in one of the three mutant heart muscle cell lines. Using cardiomyocytes derived from human induced pluripotent stem cells carrying different LMNA mutations, it was demonstrated that the effect of PTC124 is codon selective.

A premature stop codon UGA appeared to be most responsive to PTC124 treatment. This reinforces the need for precision medicine. hiPSC technology and in vitro drug testing strategies provide unparalleled opportunities to realize the promise of precision medicine. This strategy may be exploited to select the patients with maximum drug responsiveness for standard clinical trials. Then, the expected drug effects may be much larger, and the required sample size would then be much smaller, making standard randomized clinical trials possible.

While the technological breakthrough has moved the research closer to ultimate clinical uses of stem cells, the team has communicated with the drug company regarding clinical application. Meanwhile, Professor SIU and his team at the University are now building up a library of disease specific-hiPSC in order to facilitate research in understanding, treating, and preventing human diseases.

Provided by The University of Hong Kong