Genes & Diseases (2016) 3, 239–240

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://ees.elsevier.com/gendis/default.asp

RESEARCH WATCH

Mending an infarcted heart: The possibility of using iPSC technology

Fei Li

The Editorial Office of Genes & Diseases, Chongqing, 400046, China

Received 28 October 2016; accepted 2 November 2016
Available online 10 November 2016

KEYWORDS
Allogeneic;
iPSC-CM;
Monkey;
Myocardial infarction;
Transplantation

Abstract iPSCs hold great promise in that a large quantity of cardiomyocytes (iPSC-CM) can be generated and cultured in vitro for clinical purposes. These cells are currently being subjected to vigorous testing in animal transplantation models to ascertain their survivability and functional integration in the injured heart. So far, most of those studies have been conducted in small animals and sometimes in xenogeneic settings, and have produced mixed results. Representing a step forward, a recent study in *Nature* reported the transplantation of MHC-matched allogeneic monkey iPSC-CM. This was the first time iPSC-CM have been tested in a non-human primate model in an allogeneic setting, which is the next best thing to a human clinical trial.

"Mending a broken heart is never easy," or so the saying goes. This is probably also true in the case of acute myocardial infarction due to a clogged coronary artery. Although there is presently no specific treatment aimed at regenerating damaged cardiac muscle, the void is being rapidly filled, as shown by the recent developments using induced pluripotent stem cells (iPSCs). iPSCs are derived from adult tissue cells, and are transformed into pluripotent stem cells through genetic reprogramming. iPSCs hold great promise in that a large quantity of cardiomyocytes (iPSC-CM) can be generated and cultured in vitro for clinical purposes. These cells are currently being subjected to vigorous testing in animal transplantation models to ascertain their survivability and functional integration in the injured heart.[1,2] So far, most of those studies have been conducted in small animals and sometimes in xenogeneic settings, and have produced mixed results. Representing a step forward, a recent study in *Nature* reported the transplantation of MHC-matched allogeneic monkey iPSC-CM.[3] This was the first time iPSC-CM have been tested in a non-human primate model in an allogeneic setting, which is the next best thing to a human clinical trial. In that study, the authors first generated iPSC-CM using homozygous iPSC cells from cynomolgus monkeys. Homozygous stem cells have the advantage of an increased likelihood of a histocompatibility match. These homozygous iPSC-CM cells were

E-mail address: fei@genesndiseases.org.
Peer review under responsibility of Chongqing Medical University.

http://dx.doi.org/10.1016/j.gendis.2016.11.001

then transplanted into MHC-matched heterozygous monkeys modeling acute myocardial infarction. Through 12 weeks of post-transplantation observation and analysis, the authors of that study were able to show successful engraftment/survival of implanted iPSC-CM in the damaged heart. These implants were able to couple electrically and mechanically with the host cardiac muscle, which resulted in improved cardiac contraction. Another encouraging finding was that none of the five recipient animals developed tumors, which has been widely feared considering the highly proliferative potential of IPSC stem cells. However, as observed in other previous transplantation studies, all five recipient monkeys developed episodes of idioventricular arrhythmia. Fortunately, these episodes subsided in the later stage, and the recipient animals seemed to be symptom-free by the end of the study. Nevertheless, the engrafted cardiac muscles presented an immature phenotype with low expression of cardiomyocyte-specific proteins as well as a slow propagation of cardiac electric waves as suggested in previous in vitro research.[2] Since the post-transplantation analyses were only performed for 12 weeks, extended follow-up studies are warranted to investigate whether the cardiac engrafts can survive long-term, and whether they eventually mature to exhibit an appropriate phenotype.

Conflict of interest

The author declares no conflict of interest.

References

1. Medhekar SK, Shende VS, Chincholkar AB. Recent stem cell advances: cord blood and induced pluripotent stem cell for cardiac regeneration- a review. *Int J Stem Cells*. 2016;9:21—30.
2. Bedada FB, Wheelwright M, Metzger JM. Maturation status of sarcomere structure and function in human iPSC-derived cardiac myocytes. *Biochim Biophys Acta*. 2016;1863:1829—1838.
3. Shiba Y, Gomibuchi T, Seto T, et al. Allogeneic transplantation of iPS cell-derived cardiomyocytes regenerates primate hearts. *Nature*. 2016;538:388—391.