



RESEARCH WATCH

Mending an infarcted heart: The possibility of using iPSC technology



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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.

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“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

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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 idiopathic 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.

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