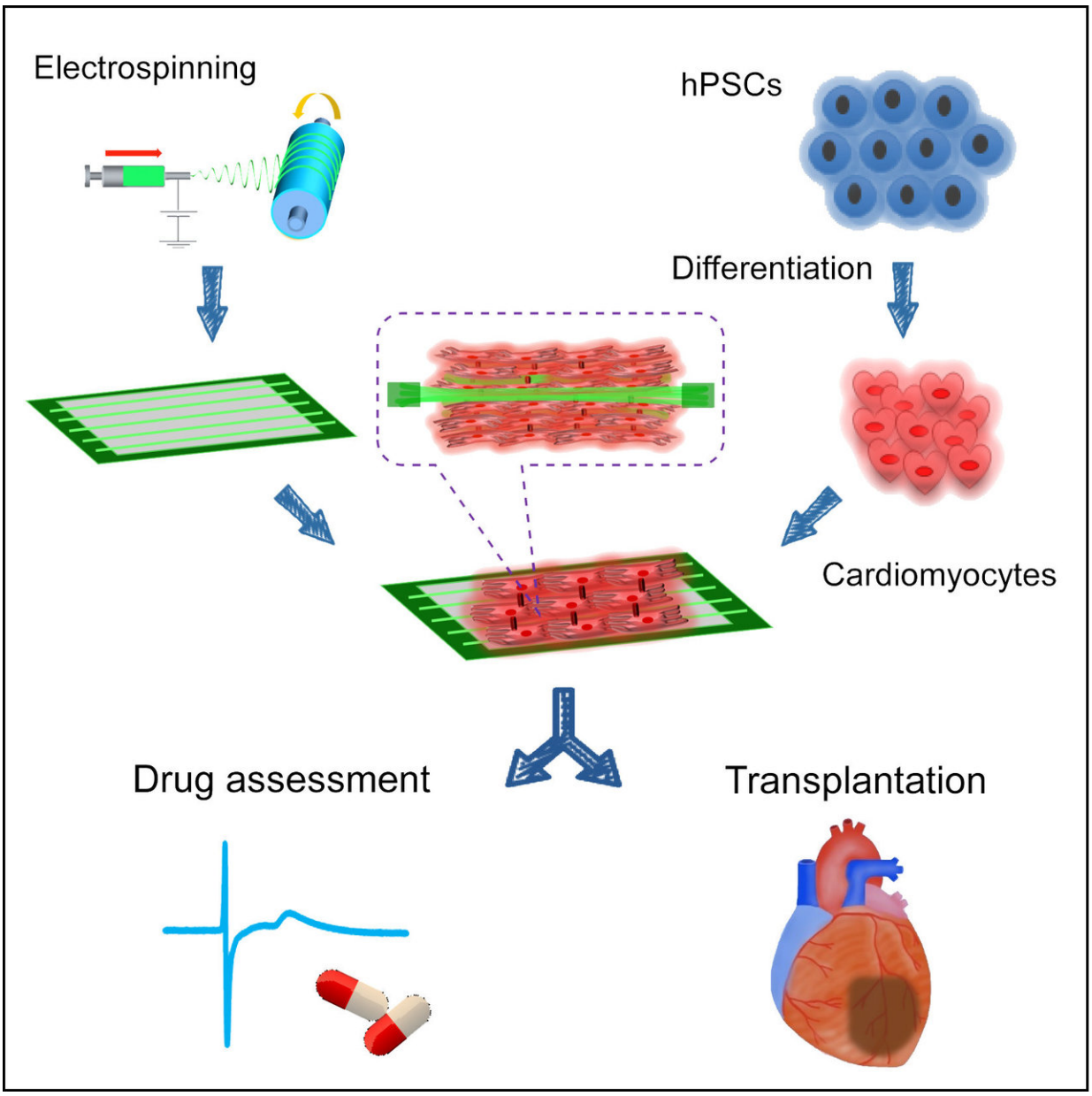
Mending hearts in three dimensions: Team uses hiPSCs to repair myocardial infarctions in rats

October 26 2017



We obtained high-quality cardiac tissue-like constructs (CTLCs) by cultivating hiPSC-CMs on aligned nanofibers made of biodegradable polymer. We show that multi-layered and elongated CMs could promptly be organized at high density along aligned nanofibers, resulting in upregulated cardiac biomarkers and enhanced cardiac functions. When used for drug assessment, CTLCs were much more robust than the 2D conventional control. We used the CTLCs to simulate the repairing of disconnected and arrhythmia CMs in vitro. When used to repair injured rat hearts, the CTLCs showed excellent operability leading to favorable heart function recovery. Credit: Kyoto University iCeMS

The creation of cardiac tissue-like constructs could offer an effective and convenient "woundplast" for repairing myocardial infarction.

Researchers from Kyoto University iCeMS and Osaka University have made biodegradable aligned nanofibers as a scaffold for culturing cardiomyocytes (CMs) derived from human induced pluripotent stem cells (hiPSCs). These CMs form myofibril-aligned, multi-layered and 3D-organized Cardiac Tissue-Like Constructs (CTLCs), which show robust drug response and may be readily used for repair of injured rat hearts with myocardial infarctions.

Researchers from the Institute for Integrated Cell-Material Sciences (iCeMS) of Kyoto University and the Department of Cardiovascular Surgery of Osaka University have developed effective and convenient Cardiac Tissue-Like Constructs (CTLCs) for repairing myocardial infarctions.

Cardiovascular diseases such as infarctions are the leading cause of death globally. A seriously injured heart cannot recover by itself, and heart transplants are the only effective treatment. However, the waiting

list for transplants is extremely long. Previous researchers have also used cell transplant technologies to repair injured hearts, but these used CMs organized in two dimensions with a random, myofibril structure, which is different from natural heart tissue.

Dr. Li Liu and Prof. Yong Chen of iCeMS, together with Prof. Yoshiki Sawa of Osaka University and colleagues, selected a PLGA material approved by the FDA, and prepared biodegradable, aligned nanofibers for culturing CMs derived from hiPSCs, successfully creating organized and functional CTLCs.

They found that the CMs infiltrated and enveloped the nanofibers, showing elongation and high organization with upregulated expression of cardiac markers. Their CTLCs demonstrated more robust drug response compared with 2D CMs.

The team also used the CTLCs to simulate the repairing of disconnected and arrhythmia CMs. When used to repair injured rat hearts, the CTLCs showed excellent operability leading to favorable heart function recovery.

Future studies are now being planned to use CTLCs to repair injured hearts of larger animals, before advancing to clinical applications.

The paper "Human Pluripotent Stem Cell-Derived Cardiac Tissue-Like Constructs for Repairing of the Infarcted Myocardium" appeared on October 26, 2017 in *Stem Cell Reports*.

Provided by Kyoto University