Innovations
UNIVERSITY OF COLORADO
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Heart regeneration by conversion of non-myocytes into functional cardiomyocytes

Category
Technology: Heart muscle regeneration
Developed: 2018

Problem
Heart Disease

Technology Overview
Conversion of fibroblasts into cardiomyocytes in situ via gene therapy

IP Status

- US patent issued
- Available for Licensing

Value Proposition

- Direct conversion to cardiomyocytes in situ
- Highly Efficient reprogramming & regeneration
- Viral vector targets fibroblasts

Market Attractions

- Myocardial infarction
- Heart failure
- Heart disease models

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Problem: Heart failure affects about 8 million Americans of all ages every year. It considerably reduces quality of life with only a 50% five-year survival rate. Recent therapeutic approaches (drug development, cell transplantation, or heart transplantation) have a limited effect on treating cardiovascular disorders. Heart diseases occur mainly because cardiomyocytes have a low regenerative capability to replace damaged heart cells. After myocardial infarction, fibroblasts represent the majority of cells in the damaged area and thus, constitute an ideal source of cells for reprogramming into cardiomyocytes. Direct reprogramming of cardiac fibroblasts to cardiomyocytes is a promising strategy that has made significant progress in the recent years. However, the main challenge remains the low efficiency of the technique.

Technical Solution and Key Value Propositions: A University of Colorado research group led by Dr. Kunhua Song has developed a new technique to restore heart function by regeneration of cardiomyocytes. The group first demonstrated that, in addition to overexpression of cardiac development transcription factors (including GATA4, Hand2, Mef2c, and Tbx5), inhibition of pro-fibrotic signaling dramatically increases reprogramming efficiency. Using the new methods, about 60% of fibroblasts express cardiac Troponin T (cTnT) and about 50% express α-actinin. Beating cardiomyocytes are observed in less than 2 weeks (Fig.1).

Dr. Song's group then effectively **converted fibroblasts into cardiomyocytes in an intact beating rodent heart** using an adeno-associated virus-based gene delivery method. About 80% of fibroblasts are transduced after a single injection. This new method allows a high conversion rate of fibroblasts into cardiomyocytes and reduces cardiac fibrosis.

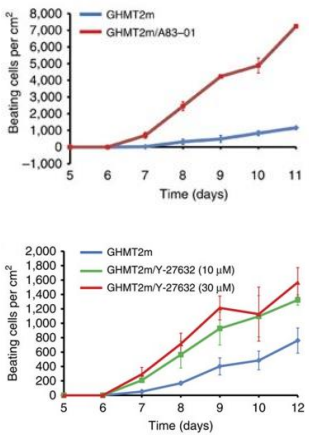

Fig. 1. Beating cell count following GHMT2m transduction and treatment with FDA approved inhibitor for TGF-β inhibitor (A83-01) or ROCK (Y-27632).

Key Documents and Sources:

1. High efficiency reprogramming of fibroblasts into cardiomyocytes. US9885018B1.
2. High-efficiency reprogramming of fibroblasts into cardiomyocytes requires suppression of pro-fibrotic signalling. Zhao Y, Londono P, Cao Y, Sharpe EJ, Proenza C, O'Rourke R, Jones KL, Jeong MY, Walker LA, Buttrick PM, McKinsey TA, Song K. Nat Commun. 2015 Sep 10; 6:8243.
3. Suppression of Pro-fibrotic Signaling Potentiates Factor-mediated Reprogramming of Mouse Embryonic Fibroblasts into Induced Cardiomyocytes. Riching AS, Zhao Y, Cao Y, Londono P, Xu H, Song K. J Vis Exp. 2018 Jun 3;(136).