Direct reprogramming of human cardiac fibroblasts to cardiomyocytes using microRNA mimics

Poster Abstract

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Abstract details	
Title	Direct reprogramming of human cardiac fibroblasts to cardiomyocytes using microRNA mimics
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The combination of four different microRNAs (miR-1, 133, 208 and 499), named "miRcombo", has been used for the direct reprogramming of murine fibroblasts into cardiomyocytes (CMs) for myocardial infarction (MI) treatments.[1,2] Here, we evaluated miRcombo mediated reprogramming of human adult cardiac fibroblasts (AHCFs) into CMs in 2D and 3D culture. After 4 days in 2D culture, ddPCR analysis showed significantly increased expression of early cardiac transcription factors (TFs) Hand2 and Mef2c ($p < 0.005$), slightly increased expression of Tbx5 and Nkx2.5 although non-significant ($p > 0.05$), and reduced Vimentin expression ($p < 0.05$) in miRcombo-transfected AHCFs compared to controls. ICC analysis showed increased expression of late cardiac markers α-sarcomeric actinin and cTnT in miRcombo-transfected AHCFs after 10 and 20 days of culture in 2D. However, ddPCR showed no significant differences of late cardiac markers Myh6 and cTnI expression between the groups after 15 days in 2D culture. On the other hand, non-transfected AHCFs cultured in 3D fibrin-based hydrogels showed enhanced cardiac TFs expression compared to 2D cultures after 4 days, while, miRcombo transfection did not significantly increase cardiac gene expression of AHCFs cultured in 3D hydrogels for 4 days. After 15 days, AHCFs cultured in 3D hydrogels showed a strongly enhanced expression of cardiac genes such as cTnI and Myh6 compared to 2D cultures. In conclusion, results showed that a 3D environment plays a key role in enhancing direct reprogramming of AHCFs into CMs.

References:
[1] Jayawardena TM et al. *Circ Res.* **2013**, *110*, 1465–1473
[2] Li Y et al. *Sci. Rep.* **2016**, *6*, 1–11

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