# Converting scar tissue to heart muscle after a heart attack

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Heart failure increases as a cause of mortality, and regenerative therapy is highly demanded. We previously demonstrated that cardiac transcription factors, Gata4, Mef2c, and Tbx5 (GMT), directly reprogrammed fibroblasts into cardiomyocytes (Ieda et al., Cell, 2010). Gene delivery of Sendai virus vectors expressing GMT in the mouse infarct hearts converted resident cardiac fibroblasts into cardiomyocytes, repaired infarct hearts, and improved cardiac function after MI (Miyamoto et al, Cell Stem Cell, 2018). We also identified a mesoderm-enriched transcription factor, Tbx6, directly induced mesoderm-like cells from fibroblasts and iPSCs, which differentiated into beating cardiomyocytes, vascular smooth muscle cells, and endothelial cells (Sadahiro et al. Cell Stem Cell, 2018). Screening of 8400 chemical compounds revealed that diclofenac (Voltaren) greatly enhanced cardiac reprogramming via suppression of inflammation and fibrosis in aged fibroblasts (Muraoka et al., Nat Commun, 2019). More recently, we have fo und that soft matrix comparable to native myocardium promoted the efficiency and quali ty of cardiac reprogramming. Mechanistically, soft matrix enhanced cardiac reprogrammin g via inhibition of YAP/TAZ and fibroblast programs, which were activated on rigid sub strates (Kurotsu et al., Stem Cell Reports, 2020). Thus, converting scar tissue to heart muscle after a heart attack may be a new approach for cardiac regeneration.