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By promoting cardiac regeneration FGF10 preserves cardiac remodeling and function after myocardial infarction

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In mammals, cardiomyocyte proliferation decreases rapidly after birth resulting in severely limited regenerative capacities in the adult heart. Deciphering developmental mechanisms involved in cardiomyocyte proliferation may thus identify new therapeutic targets to modulate cell cycle activity of adult cardiomyocytes which therefore may promote cardiac regeneration. We recently identified the role of the Fibroblast Growth Factor 10 (FGF10) in the regulation of both fetal and adult cardiomyocyte proliferation thus revealing FGF10 as a potential relevant target to promote cardiomyocyte cell cycle reentry after cardiac injury.

Using an experimental mouse model of myocardial infarction (MI), together with Fgf10 loss and gain of function mouse models, we investigated the role of FGF10 in pathological conditions. We first showed that MI leads to increased Fgf10 expression levels in cardiomyocytes of the injured ventricle suggesting a potential role for FGF10 in pathological conditions. In order to determine a potential protective role of FGF10 under pathological conditions, adult transgenic mice with reduced Fgf10 expression were subjected to MI. Our results revealed that while reduced Fgf10 expression has no impact on cardiomyocyte hypertrophy and apoptosis, it significantly impairs cardiomyocyte proliferative capacities and exacerbates cardiac fibrosis infiltration post-MI. Moreover, echocardiographic experiments showed that reduced Fgf10 expression leads to a worsened cardiac function and remodeling post-MI, strongly demonstrating the protective role of FGF10 in pathological conditions. In order to estimate the regenerative capacities of FGF10 in pathological conditions, we investigated whether FGF10 can rescue cardiac function following MI. To this end, conditional Fgf10 overexpression was achieved in adult mice subjected to MI. Three weeks after MI, cell proliferation, cardiac fibrosis and heart function were evaluated. Our preliminary experiments indicate that by promoting cardiomyocyte proliferation and preventing cardiac fibrosis infiltration, increased Fgf10 expression levels post-MI preserves cardiac remodeling and function.

Altogether, this study thus identifies FGF10 as a potential target to improve the limited innate regenerative capacities of the myocardium after injury, of direct clinical relevance for heart repair.