

Table 4 Pre-clinical studies on targeted growth factor delivery systems for cardiac repair

Growth Factor	Delivery System	Animal model	Route	Effect	Reference
FGF-1	Peptide nanofibers	Acute MI in SD rats	IM	Treatment with FGF-1+p38 MAP kinase inhibitor: increased cardiomyocyte mitosis; reduced scarring and wall thinning with markedly improved cardiac function	[140]
	Slow release pump	Chronic MI in pigs	Perivascular space	Improved perfusion in the LCx region, but no significant blood flow in the LAD territory; no cardiac function and histology assessments	[141]
FGF-2	<i>p</i> (NIPAAm-co-PAA-co-BA) hydrogel	Acute MI in Fischer rats	IM	Improved angiogenesis and regional blood flow, but chronic inflammatory response observed near the polymer injection site	[139]
	Gelatin hydrogel	Chronic MI in Lewis rats	IM	Functionally significant angiogenesis and improved LV function	[142]
	Chitosan hydrogel	Acute MI in SD rats	IM	Recovered LVEF, enhanced arteriole density and significantly reduced infarct size and fibrotic area	[124]
	Chitosan hydrogel	Chronic MI in rabbits	Surface of the ischemic myocardium	Increased angiogenesis and evidence of enhanced collateral circulation in the ischemic myocardium	[123]
	Gelatin hydrogel	Acute MI in SD rats	IM	Improved vessel density; no differences in infarct size and fibrosis among the groups; no improvements on cardiac function	[143]
	Gelatin hydrogel microspheres	Chronic MI in pigs	IM	Positive LV remodeling and improved vascular density	[144]
	Anti-P-selectin-conjugated liposomes	Acute MI in SD rats	Tail-vein injections	Significant increase in tissue vascularization; no evidence of mature of angiogenic response	[145]
VEGF-A	Fusion Protein with a collagen-binding domain	Acute MI in SD rats	IM	Increased capillary density; no evidence of vasculogenesis	[146]
	<i>p</i> (PVL-b-PEG-b-PVL) hydrogel	Subacute MI in SD rats	IM	Attenuated adverse cardiac remodelling and improved ventricular function	[147]
	PLGA microparticles	Acute ischemia–reperfusion in SD rats	IM	Increased angiogenesis and arteriogenesis; a positive remodeling of the heart was also detected in the VEGF-A-microparticle group with a significantly greater LV wall thickness	[130]
	Core/shell nanoparticles	Subacute MI in SD rats	IM	Improved heart functions (ejection fraction and cardiac output)	[148]

VEGF-A/PDGF-BB	Alginate hydrogel	Subacute MI in Fisher rats	IM	Higher vessel density with sequential GF delivery than single factors; no increment in capillary density with sequential delivery of both proteins in alginate	[117]
EPO	cyclodextrin/MPEG-PCL-MPEG hydrogel	Acute MI in SD rats	IM	Reduced infarct size and improved cardiac function without evidence of polycythemia	[149]

FGF-1: acidic Fibroblast Growth Factor; FGF-2: basic Fibroblast Growth Factor; VEGF: Vascular Endothelial Growth Factor; PDGF: Platelet-derived Growth Factor; EPO: Erythropoietin; MI: myocardial infarction; SD: Sprague-Dawley; IM: Intramyocardial; LAD: Left anterior descending coronary artery; *p*(NIPAAm-co-PAA-co-BA): poly(N-isopropylacrylamide-co-propylacrylic acid-co-butyl acrylate); LVEF: left ventricle ejection fraction; *p*(PVL-b-PEG-b-PVL): poly (d-valerolactone)-block-poly (ethylene glycol)-block-poly (d-valerolactone); PLGA: poly(lactic-co-glycolic acid); MPEG-PCL-MPEG: [methoxy polyethylene glycol-poly(caprolactone)-(dodecanedioic acid)-poly(caprolactone)-methoxy polyethylene glycol] triblock polymer.