Electronic Supplementary Material (ESI) for Biomaterials Science.

Supporting Information

Table S1: Reinforcing agents used in electrospun mats and hydrogels

Polymer/(s)	Nanofiller	Mechanical Performance	Refs
Electrospun mats			
poly (lactic acid) (PLA)/polyvinylpyrrolidone (PVP)	MWCNTs	Young's modulus of PLA/PVP: 1.5± 0.25 GPa Young's modulus of PLA/PVP/MWCNTs: 3.27± 0.20 GPa	1
PLGA/ silk fibroin	GO nanosheets	2.8 fold increase in Young's Modulus	2
PLA	Hydroxyapatite (HA)	Increase of the elastic modulus by ~130-170 %	3
PLLA	Montmorillonite	Increase in stiffness of MMT/PLLA nanocomposites by 40% compared with pristine PLLA	4
PCL/Gelatin	Cellulose NFs	ultimate tensile strength of the PCL/Gel was remarkably enhanced from 2.5 ± 0.1 MPa to 4.3 ± 0.1 MPa	5
Chitosan/PEO	Bioactive glass	889% increase in tensile strength compared to unmodified scaffold	6
Hydrogels			
Poly(acrylamide-co-acrylic acid) (PCS)	chitosan decorated halloysite nanotubes	Tensile strength of composite: 2.63 MPa Tensile strength of PCS: 1.03 MPa Toughness of composite: 33.71 MJm-3 Toughness of PCS: 7.79 MJm-3	7
Sodium alginate (SA)	carbon nanofibers (CNFs)	Compression modulus of SA: 1.2 kPa Compression modulus of SA+2% CNFs: 10 kPa	8
sodium carboxymethyl cellulose and chitosan	halloysite nanotubes (HNTs) and graphene oxide (GO)	Stiffness of CMC-CS: 675 N/m Stiffness of CMC-CS+ HNTs/GO: 2200 N/m	9

chitosan	Cellulose nanofibers	20 % increase in compressive strength	10

Table S2: Summary of electroconductive biomaterials used for repair and restoration of myocardial tissue

Electroconductive material	Cardiac Patches		Injectable hydrogels	
	Polymer matrix	Main findings	Polymer matrix	Main findings
CNTs	Chitosan/PVA	↑in the expression of Nkx2.5, Troponin I, and β–MHC cardiac markers (11)	Gelatin	↑cTnT and Cx43 in vitro (improved cardiac cell function), angiogenesis in vivo (12)
Graphene	Collagen	upregulated cardiac gene expression involve in electrical coupling (Cx43), muscle contraction and relaxation (troponin-T) and cytoskeleton alignment (actinin-4) (13)	gelatin methacryloyl (GelMA)	Enhanced the electrical conductivity, improved contractility and induced faster spontaneous beating rate of cardiomyocytes in vitro (14)
Polyaniline (PANI)	poly(glycerol-sebacate)	Good attachment, growth and proliferation of C2C12 myoblasts (15)	collagen, fibroin solution, hyaluronic acid	Supported viability and proliferation of cardiomyocytes (16)
Polypyrole (PPy)	chitosan	mimics the mechano-electronic function for cardiomyocytes maturation and integrity. Triggers angiogenesis and promotes cardiac pumping performance in the infarcted area (17)	Chitosan	Improved electric conduction in vivo as shown by decreased QRS interval and increased transverse activation velocity in comparison with pure chitosan (18)
Au nanomaterials	Polyurethane	Upregulation of gene expression levels of Nkx2.5, atrial natriuretic peptide (ANF) and natriuretic peptide precursor B (NPPB) (19)	polyethylene glycol diacrylate/4-vinyl phenylboronic acid (PEGDA-PBA) and thiol hyaluronic acid (HA-SH)	upregulated infarct margin angiogenesis, reduced cell apoptosis, and increased an expression of Connexm43 (Cx43) (20)

Table S3: Summary of studies involving the use of cardiac patches for myocardial repair

Cell source/ cell number	Bioactive molecule	Scaffold material	Diameter, pore size, porosity	Animal model	Follow up	Heart function e.g improved LVEF	Other observations	Refs
cardiosphere-derived stromal cells 2.0×10^5 cells	fibrinogen thrombin aprotinin	Fibrin gel	-	Rat and porcine	4 weeks	Promoted cardiac function recovery and limited pathological ventricular remodeling	Increase in cardiomyocyte proliferating, new blood vessel formation, endogenous progenitor cell activation, and alleviation of pro-inflammatory cytokine expression	21
Neonatal rat ventricular myocytes 40,000 cells/cm2	Au NPs (43 nm)	Collagen patch	Fiber diameter ≈ 1.6 μm	C57BL/6 mice	28 days	Improved LVEF Net decrease in scar size Increase in vascular density	• Improved electrical conductivity • Increased vasculogenesis within the infarcted area	22
neonatal rat cardiomyocytes ;1.5×104 cells per cm2 HUVECs; 104 cells per cm2	Si ions	Chitosan /Calcium Silicate	FD: 200 -300 nm	Rats	6 weeks	limited the scar area and promoted angiogenesis in vivo	Si ions stimulated the expression of cardiac specific genes and proliferation of neonatal rat cardiomyocytes (concentration range 0.13 ~ 10.78 ppm) Improved myofilament structure	23
NA	NA	chitosan	-	Rats	8	Reduced the	Improved VEGF, bFGF and	24

		- hyaluronan/silk fibroin			weeks	dilation of LVs, increased the thickness of their walls and improved the fractional shortening (LVFS)	HGF secretion in the MI region	
human cardiac-derived progenitor cells (30×10^6 cells/ml)	NA	gelatin/hyaluronic acid	-	Mice	4 weeks	a significant reduction in EDV and ESV improved cardiac remodeling + decreased infarct fibrosis Increased infarct wall thickness	• Allowed hCMPC attachment and proliferation • hCMPC retained their cardiogenic phenotype in vitro up to 1 month	25
NA	NA	polyester urethane urea (PEUU)	91% porosity and a 91-μm average pore size tensile strength: 0.78 MPa elongation at rupture:	Rats	8 weeks	Thicker and denser ventricular wall with muscle-like bundles compared to the control Significant increase in end-diastolic LV cavity area (EDA) improved contractile function	In vivo infiltration of patch with macrophages and fibroblasts.	26

			157%.					
mesenchymal stem cells 2×105cells/ 8×8mm2 patch	NA	Chitosan /silk fibroin	FD: 230-475 nm Pore size: 4300-550 nm	Rats	28 days	EF and FS were improved EDV and ESV decreased markedly decreased fibrosis and scar size improved contractility and relaxation Promoted angiogenesis	Active proliferation of MSCs	27

Table S4: : Summary of studies involving the use of hydrogels for myocardial repair

Cell source/ cell number	Bioactive molecule	Hydrogel material	Animal model	Follow up	Heart function e.g improved LVEF	Other observations	Refs
hiPSCs-CMs and hiPSCs-SCs mixed in a 80:20 ratio Total of 10000 living cells	none	poly(NIPAAm-co-HEMA-co-MAPLA)	Lewis rats Yorkshire swine	8 weeks	• Reduced scarring in porcine LV myocardium • Cardiac function improvements • Attenuated left ventricular remodeling, even after significant hydrogel degradation had occurred in vivo	• Stiffened ventricular wall in both circumferential and longitudinal directions with similar stiffness compared to healthy control • Cell infiltration and tissue integration into degraded hydrogel. • Higher level of vasculature was found in hydrogel treated hearts compared to PBS control	10.1016/j.biomaterials.2019.119289
human umbilical mesenchymal stem cell (hUMSC) 1×10^8	none	collagen	minipigs	12 months 8	Higher left ventricular ejection fraction (LVEF) and lower infarct size percentage	• Improved cardiac output • Intramyocardial retention of hUMSCs and artery renewal, neoangiogenesis in infarct zone	10.1007/s11427-019-1575-x
NA	bFGF	gelatin	Mongre	2	• increase of		Jpn Circ J

			l dogs	weeks	vascular density in the ischemic region • improved collateral circulation to the infarct area		2001; 65: 439 – 444
NA	salvianolic acid B loaded polydopamine nanoparticles	elastin-mimic peptide	Rats	4 weeks	• Inhibit ventricular remodeling • Restoration of cardiac function as shown by extensive angiogenesis in the MI area	• Reduced fibrosis and wall thinning • Minimal apoptosis of cardiomyocytes compared to negative control	10.1016/j.biomaterials.2021.120855
NA	Platelet rich fibrin (Ly-PRF)	Alginate-hyaluronic acid	Rats	4 weeks	Preserved heart function and the Ly-PRF within the hydrogel promoted angiogenesis and increased vascular density in both infarcted and border	Macrophage polarization: increased number of CD163-positive cells in the infarct and border zones Reduced of myocardial fibrosis	10.1016/j.bioactmat.2021.05.042

					zone	Sharp increase in LV anterior wall thickness Few apoptotic cells	
NA	dimeric fragment of hepatocyte growth factor (HGFdf) and engineered stromal cell-derived factor 1α(ESA)	Hyaluronic acid	Wistar rats Dorset sheep	8 weeks	Significantly reduced infarct and scar size Improvement in LV geometric parameters and functions	Significant increase in arteriole density within the border zone region	10.1016/j.cyto.2019.154974

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