Table 1. Summary of the animal studies eligible for this review.

Species	Type of model	Target Organ	Mitochondrial source of donor	Transplantation method and timing	Randomization	Blinded assessment	Main outcomes	Ref.
C57BL6 mice (male)	Focal ischemia (MCAO)	Brain	Allograft: Placenta	IV, Immediately after reperfusion	Yes	Yes	Decreased infarct size 72 h post-ischemia	[25]
Wistar rat	Focal ischemia (MCAO)	Brain	Xenograft: hUC-MSCs	Direct ICVs, After reperfusion (within 10 min)	Not reported	Not reported	Reduced Infarct size 72 h after ischemia; Improved motor function after 24 h	[31]
SD rat (male)	Focal ischemia (MCAO)	Brain	Autograft: Pectoralis major muscle	Direct ICVs, Immediately after reperfusion	Yes	Yes	Improved motor functions after MCAO, with reduced infarct volume and apoptosis	[32]
SD rats (male)	Focal ischemia (MCAO)	Brain	Xenograft: BHK-21 cells	Direct IC or IA (femoral), 24 h post-MCAO	Not reported	Not reported	IC and IA reduced infarct size 4 weeks post-ischemia and improved functional rotarod and grip strength performance for up to 1-month post-transplantation	[33]
1) bEnd3 and PC12 cell 2) C57BL6 mice (male)	1) OGD, 2) TBI	1) Cell, 2) Brain	Allograft: BDMts	1) Coculture 2) IC into the ipsilateral cortex, 10 min post-TBI	Yes	Yes	1) *In vitro*: improved cellular respiration and synaptic plasticity 2) *In vivo*: Reduced apoptosis, BBB damage, and brain edema	[30]
Yorkshire pigs (female)	Focal ischemia	Heart	Autograft: Pectoralis major muscle	IA (coronary), 120 min after reperfusion	Yes	Not reported	Reduced myocardial infarct size and enhanced regional and global myocardial	[34]

							function post-reperfusion	
Yorkshire Pigs (female)	Focal ischemia	Heart	Autograft: Pectoralis major muscle	Subendocardial injection 8 times, 1 min before reperfusion	Yes	Not reported	No change in inflammatory and cytokine activation markers; decreased infarct size but no change in global function	[36]
Yorkshire swine (female)	Focal ischemia	Heart	Autograft: Pectoralis major muscle	IA (coronary), Immediately on reperfusion	Not reported	No	Improved myocardial function, perfusion, and infarct size	[37]
Yorkshire Pigs (female)	Focal ischemia	Heart	Autograft: Pectoralis major muscle	Single IA (coronary): 15 min before regional ischemia. Serial IA (coronary): every 5 min since 60 min before ischemia	Yes	Yes	Reduced myocardial infarct size, improved myocardial function; no difference between single and serial injections	[38]
New Zealand White rabbits (female)	1) Image study: Global or regional ischemia 2) Function study; regional ischemia	Heart	1) Xenograft: Human cardiac fibroblasts 2) Autograft: Liver	1) direct injection or IA (coronary), upon reperfusion 2) IA (coronary), upon reperfusion	Not reported	Yes	1) Mitochondria were observed in interstitial spaces, associated with blood vessels, and cardiomyocytes 2) Reduced infarct size and enhanced myocardial function	[39]
New Zealand white rabbits (male)	Focal ischemia	Heart	Autograft: Pectoralis major muscle	Direct injection 8 times, 1 min before reperfusion	Not reported	Yes	Reduced myocardial infarct size and enhanced regional myocardial function post-reperfusion	[40]
C57BL/6J mice (male)	Focal ischemia	Heart	Allograft: Gastrocnemius muscle	IA (coronary), 10 min before organ harvest and 5 min after	Not reported	Yes	Enhanced graft function and decreased graft tissue injury	[41]

				transplantation				
C57BL/6 mice (male)	Focal ischemia	Heart	Not reported	Direct injection at myocardium of the left ventricle, during 24 h perfusion at 4 different points.	Not reported	Not reported	Mitochondrial transplantation inhibited cardiomyocyte apoptosis in vitro. In vivo transplantation of Alda-1-treated mitochondria limited infarction size after I/R injury.	[42]
Yorkshire pigs (female)	Global ischemia	Heart	1) 1st, Autograft: Pectoralis major muscle 2) 2nd, Allograft: swine cardiac fibroblast cell	IA (coronary), 1) 15 min post-reperfusion 2) 2 h post-reperfusion	Yes	Yes	Preserved myocardial function and oxygen consumption and, decreased infarct size	[35]
Wistar rats (male)	Focal ischemia	Kidney	Autograft: Pectoralis major muscle	IA (renal), 5 min before reperfusion	Not reported	Not reported	Increased renal function, renal cell repair, and proliferation capacity	[43]
Yorkshire pigs (female)	Focal ischemia	Kidney	Autograft: Sternocleidomastoid muscle	Single IA (renal artery), Immediately at reperfusion	Yes	Yes	No safety issues detected. Increased GFR and urine output, decreased serum creatinine and BUN	[44]
C57BL/6J mice (male)	Focal ischemia	Hindlimb	Allograft: Muscle	Direct injection, 15 min after reperfusion	Not reported	Yes	Decreased infarct size and apoptosis; improved hindlimb function	[45]
C57BL/6J mice (male)	Focal ischemia	Lung	Allograft: Gastrocnemius muscle	IA (pulmonary) or Aerosol delivery to whole lung by nebulization, Immediately at reperfusion	Yes	Yes	Both delivery methods improved lung mechanics and decreased lung tissue injury	[46]
SD rats (male)	Focal ischemia	Spinal cord	Allograft: Soleus muscle	IV (jugular), 5 min before reperfusion	Yes	Yes	Attenuated inflammatory, ER stress, and neuro-apoptotic reactions. Improvement in motor function	[47]

SD rats (male)	Focal ischemia	Liver	Allograft: Liver	Portal vein, upon reperfusion	Yes	Not reported	^{31}P-MRS showed that the hepatic levels of ATP and NADH were higher in the m-Mito group than in the IRI group. The m-Mito group decreased the liver injury score and inflammatory cell infiltration in liver compared to the IRI group	[48]

SD, Sprague–Dawley; hUC-MSCs, human umbilical cord derived mesenchymal stem cells; MCAO, middle cerebral artery occlusion; OGD, glucose oxygen deprivation; TBI, traumatic brain injury; BHK-21, Baby hamster kidney fibroblast; BDMt, brain-derived mitochondria; ICV, intracerebroventricular injection; IC, intracerebral injection; IA, intra-arterial injection; BBB, blood brain barrier; GFR, glomerular filtration rate; BUN, blood urea nitrogen; ER, endoplasmic reticulum; IRI, ischemia reperfusion injury; ^{31}P-MRS, ^{31}P-magnetic resonance spectroscopy; m-Mito, melatonin pretreated-mitochondrial transplantation