Supplementary material: A summary of the preclinical and clinical (grey) studies on the application of stem cells to promote tendon repair.

Ref	**Stem cell type**	**Type of tendon injury**	**Species**	**Scaffold**	**Pretreatment *in vitro***	**Longest FU**	**Findings**
1	Allogeneic rat BMSCs	Achilles tendon transection	Rat	Serum	Nil	8 weeks	The BMSC-serum group showed higher tensile strength and lower apoptosis compared to the serum-only group. There was no significant difference in histology between the BMSC-serum group and serum-only group.
2	Allogeneic rat BMSCs	Achilles tendon transection	Rat	PBS	+/- Hypoxic pretreatment (1% O_2)	4 weeks	Hypoxic BMSCs promoted better tendon repair compared to normoxic BMSCs and PBS-only control as shown by biomechanical test and histology. The expression of collagen type I and type III were stronger in the hypoxic and normoxic MSC groups compared to the PBS-only control group.
3	Allogeneic rat BMSCs	Achilles tendon transection	Rat	Suture coated with ICAM-1 and poly-L-lysine	Nil	4 weeks	The BMSC-coated suture group improved the strength of the healing tendons at day 7 and day 10 but not at the later time points compared to the suture-only group.
4	Autologous rat BMSCs	Achilles tendon transection	Rat	PBS	+/- Overexpression of bFGF	4 weeks	The injection of BMSCs overexpressing eGFP or BMSCs overexpressing bFGF did not improve the histology and expression of tendon-related ECM protein except procollagen type I, and have negative effects on the biomechanical properties of the healing tendons at week 4 compared to the injection of PBS. Overexpression of bFGF in BMSCs had negligible effects on tendon healing.
5	Autologous rat whole bone marrow cells or BMSCs	Achilles tendon transection	Rat	DMEM	Nil	5 weeks	The bone marrow group showed higher ultimate load, immunohistochemical staining of collagen type I and collagen type III as well as mRNA expression of TGF- β and VEGF compared to the cultured BMSC group which in terms was higher than the untreated group up to week 4.
6	Allogeneic	Achilles tendon transection	Rabbit	Fibrin glue	Nil	12 weeks	The transplantation of BMSCs in fibrin glue promoted early stage (3 weeks) of tendon

	rabbit BMSCs						repair but not at later stages compared to the fibrin glue-only group as shown by histology and biomechanical test.
7	Human BMSCs	Achilles tendon segmental defect	Rat	Suture	Nil	4 weeks	Both the suture+BMSC injection group and the suture-loaded BMSC group showed higher ultimate failure strength compared to the suture-only group, and the strength was maintained at 4 weeks in the suture-loaded BMSC group but not in the suture+BMSC group. Histology of the healing tendons in the suture-loaded BMSC group was better than that in the other groups.
8	Autologous rat BMSCs	Achilles tendon segmental defect	Rat (inbred)	PGA or collagen type I	Nil	16 weeks	Except more inflammation associated with the use of PGA, similar findings were observed for the use of PGA or collagen type I as the scaffold for cell transplantation. Ectopic ossification was observed in all groups. The transplantation of tenocytes seeded in either scaffold improved the biomechanical properties and grade of ectopic ossification of the healing tendons compared to the BMSC-transplanted groups and the scaffold-only groups. The transplantation of BMSCs seeded in either scaffold did not promote better tendon repair compared to the scaffold-only groups.
9	Autologous rabbit BMSCs	Achilles tendon segmental defect	Rabbit	PGA-collagen	Nil	12 weeks	The transplantation of BMSCs seeded in PGA-collagen scaffold promoted better tendon repair compared to the scaffold-only group as shown by histology.
10	Autologous rabbit BMSCs	Achilles tendon segmental defect	Rabbit	Silk-fibroin-PLGA mesh filled with collagen type I	Nil	16 weeks	The transplantation of BMSCs seeded in scaffold promoted better biomechanical properties and histology of the healing tendons compared to the scaffold-only group. There was no difference in the mRNA expression of collagen type I and collagen type III between the BMSCs seeded in scaffold group and scaffold-only group.
11	Autologous rabbit	Achilles tendon segmental defect	Rabbit	Collagen gel	Contracted on a tensioned suture	12 weeks	The transplantation of BMSCs seeded in collagen gel promoted higher structural and material properties as well as better collagen fiber alignment compared to the

	BMSCs				for 40 hours		suture-only group
12	Autologous rabbit BMSCs	Achilles tendon segmental defect	Rabbit	Alginate gel encapsulating PLGA knitted structure	Nil	13 weeks	The group with the transplantation of BMSCs seeded in scaffold (BMSC group) presented higher normalized elastic modulus compared to the natural healing group and scaffold-only group. Histology showed higher cell density and vascularization in the healing tendons in the BMSC group compared to the natural healing group.
13	Allogeneic rabbit bone marrow stromal cells	Achilles tendon segmental defect	Rabbit	Knitted PLGA and fibrin glue	Nil	12 weeks	The transplantation of bone marrow stromal cells seeded in fibrin glue + knitted PLGA scaffold promoted better tendon repair compared to the fibrin glue + PLGA scaffold-only group as shown by better histology and higher stiffness but not elastic modulus of the healing tendon.
14	Rabbit bone marrow stromal cells (not mentioned autologous or allogeneic)	Achilles tendon segmental defect	Rabbit	Knitted PLGA and fibrin glue	Nil	12 weeks	The transplantation of BMSCs seeded in fibrin glue + PLGA scaffold promoted better tendon repair compared to the fibrin glue + scaffold-only group as shown by more mature collagen fibers in the healing tendon at week 4.
15	Allogeneic rat BMSCs	Achilles tendon partial segmental defect	Rat	Collagen sponge	+/- Pretreatment with BMP-12	3 weeks	The transplantation of BMSCs pretreated with BMP-12 in collagen sponge promoted better tendon repair compared to the transplantation of untreated BMSCs in collagen sponge which in turns was better than the collagen sponge-only group as shown by histology; immunohistochemical staining and mRNA expression of tendon-related markers.
16	Allogeneic rat BMSCs	Achilles tendon partial segmental defect	Rat	Bovine deep flexor tendon collagen scaffold	Nil	3 weeks	The transplantation of BMSCs seeded in scaffold enhanced tendon repair as shown by histology and higher gene expression of tendon-related markers compared to the scaffold-only group
17	Autologous	Achilles tendon partial	Rabbit	Collagen gel	Cell traction	12 weeks	There was no significant difference in the biomechanical properties and

	rabbit BMSCs	segmental defect			forces induced by culturing constructs between posts for 2 weeks		immunohistochemical staining of tendon-related ECM proteins of the healing tendons after BMSC transplantation at the two tested cell-to-collagen ratios (0.04 and 0.08 $x10^6$ cells/mg).
18	Rabbit BMSCs (not mentioned autologous or allogeneic)	Achilles tendon window injury	Rabbit	Not mentioned	+/- Overexpression of TGF-β1	8 weeks	The transplantation of BMSCs overexpressing TGF-β1 improved the histology, immunohistochemical staining of collagen type I and biomechanical properties of the healing tendons compared to the transplantation of non-transduced BMSCs.
19	Allogeneic rabbit BMSCs	Achilles tendon window injury	Rabbit	Fibrin glue	+/- Overexpression of TGF-β1, VEGF165 or both	8 weeks	The transplantation of BMSCs overexpressing TGF-β1 or TGF-β1/VEGF165 in fibrin glue promoted better tendon repair histologically and biomechanically compared to the other groups, while the transplantation of BMSCs overexpressing VEGF165 in fibrin glue had a negative effect on tendon repair. In the TGF-β1/VEGF165 in fibrin glue group, the angiogeneic effect of overexpressing VEGF165 in BMSCs was diminished by the overexpressing TGF-β1, while collagen synthesis induced by overexpressing TGF-β1 in BMSCs was unaltered by the overexpression of VEGF165.
20	Human BMSCs	Patellar tendon window injury	Rat (immunodeficient)	Fibrin glue	Nil	20 days	The BMSCs in fibrin glue group showed more mature tissue formation in histology compared to the defect-only and fibrin glue-only groups.
21	Human BMSCs	Patellar tendon window injury	Rat (immunosuppressed)	Fibrin glue	Nil	20 days	The BMSCs in fibrin glue group showed more mature tissue formation, larger collagen fibril diameter and area compared to the defect-only and fibrin glue-only groups. The collagen I mRNA expression, collagen I/collagen III mRNA ratio and Young's modulus in the BMSCs in fibrin glue group were higher compared to the defect-only and fibrin glue-only groups. The transplantation of fibroblasts in fibrin glue showed minimal

							effects on tendon healing.
22	Autologous rabbit BMSCs	Patellar tendon window defect (extended into the bone)	Rabbit	Collagen gel	Cell traction forces induced by culturing constructs between posts for 2 weeks	12 weeks	There was no significant difference in the biomechanical properties and histological appearance of the healing tendons among the two tested cell-to-collagen ratio (0.04 and 0.08 $x10^6$ cells/mg) in scaffold groups and the two scaffold-only groups. The repaired tissue has low stiffness.
23	Autologous rabbit BMSCs	Patellar tendon window injury	Rabbit	Collagen gel	Contracted on a suture for 24 hours	12 weeks	The age of BMSCs used for transplantation (1 year versus 4 years) did not affect the structural and material properties of the healing tendons. Ectopic bone was formed in the repair region in a subset of animals after the transplantation of old and younger stem cells.
24	Autologous rabbit BMSCs	Patellar tendon window injury	Rabbit	Collagen gel	Nil	4 weeks	The transplantation of BMSCs seeded in collagen gel promoted better tendon repair as shown by better biomechanical properties of the healing tendons compared to the collagen gel-only group. However, there was minor or no histological and morphometrical improvement in the BMSCs seeded in collagen gel group compared to the collagen gel-only group.
25	Autologous rabbit BMSCs	Patellar tendon window injury	Rabbit	Collagen sponge +/- additional dehydrothermal crosslinking	Tensile loading at 2.4% strain, 8h/day for 12 days at 100 cycles/day or 3000 cycles/day	12 weeks	Increasing the *in vitro* cycle numbers delivered to the BMSC-collagen sponge constructs used for transplantation did not change the biomechanical properties and histology of the healing tendons. Cross-linking of collagen in the scaffold lowered the stiffness of the healing tendons compared to a previous study.
26	Autologous rabbit BMSCs	Patellar tendon window injury	Rabbit	Collagen gel plus collagen sponge	+/- Tensile loading at 2.4% strain, 1 Hz cycle	12 weeks	*In vitro* loading of BMSC-collagen gel-collagen sponge constructs prior to transplantation improved the structural and material properties of the healing tendons compared to the unloaded BMSC-collagen gel-collagen sponge group.

					every 5 min, 8h/day for 2 weeks		
27	Autologous rabbit BMSCs	Patellar tendon window injury	Rabbit	Collagen sponge	+/- Tensile loading at 4% strain, once every 5 min, 8h/day for 2 weeks	12 weeks	*In vitro* loading of BMSC-collagen sponge constructs prior to transplantation significantly improved the biomechanics of the healing tendons but has no observable differences in histology compared to the unstimulated BMSC-collagen sponge group.
28	Autologous rabbit BMSCs	Patellar tendon window injury	Rabbit	Collagen gel - collagen sponge composite	Nil	12 weeks	The transplantation of BMSCs seeded in scaffold enhanced the biomechanics of the healing tendons but has no observable difference in ECM staining compared to the scaffold-only group. The transplantation of BMSCs seeded in scaffold also enhanced cell alignment which was comparable to that of the normal tendon.
29	Autologous rabbit BMSCs	Patellar tendon window injury	Rabbit	Collagen gel	Contracted on tensioned suture for 40h	26 weeks	The transplantation of BMSC-collagen gel composites improved the biomechanical properties but has no significant effects on the cellular organization and histological appearance of the healing tendons compared to the natural repair group. 28% of repaired tendon formed bone in the BMSC-collagen gel group and did not correlate with the seeding density and time post-implantation. Increasing the BMSC concentration did not produce additional histological or biomechanical benefits on the healing tendons.
30	Autologous rabbit BMSCs	Patellar tendon window injury	Rabbit	Collagen gel	Nil	4 weeks	The transplantation of BMSCs seeded in collagen gel improved the biomechanical properties but did not produce visible improvement in histomorphometry and histology of the healing tendons compared to the collagen gel-only control.
31	Autologous rabbit BMSCs	(1) Patellar tendon window injury (2) Achilles tendon	Rabbit	(1) Collagen gel (2) Collagen gel	(1) Nil (2) Contracted on tensioned suture	Part I: 4 weeks Part II: 12 weeks	(1) The BMSC-collagen gel group showed better material properties of the healing tendons compared to the collagen gel-only group. (2) The transplantation of BMSC-collagen gel constructs contracted on a tensioned

		segmental defect			for 40h		suture showed better structural and material properties of the healing tendons compared to the suture-only group.
32	Autologous rabbit BMSCs	Rotator cuff tendon window injury	Rabbit	Open-cell polylactic acid (OPLA)	Nil	6 weeks	The transplantation of BMSCs seeded in OPLA promoted better tendon repair as shown by higher cellularity, more organized collagen fibers and higher immunohistochemical staining of collagen type I in the healing tendons compared to the OPLA-only group.
33	Autologous horse BMSCs	SDFT core defect	Horse	Autologous bone marrow supernatant	Nil	12 weeks	The injection of BMSCs in bone marrow supernatant did not change the fibril diameter and distribution in the healing tendons compared to the injection of only bone marrow supernatant.
34	Human BMSCs	Collagenase-induced Achilles tendon injury	Rat (immunosuppressed)	Human mixed platelet lysate	Nil	6 weeks	The injection of BMSCs in platelet lysate promoted better vascularization, ECM deposition and organization in the healing tendons compared to the saline group. Cartilage and bone were formed at a higher frequency at the implantation site in the BMSCs in platelet lysate group compared to the saline group at 6 weeks after injury.
35	Allogeneic sheep BMSCs	Collagenase-induced Achilles tendon injury	Sheep	Fibrin glue	Nil	6 weeks	The injection of BMSCs in fibrin glue promoted tendon healing and high expression of CD34+ cells in the treated tendon compared to the injection of fibrin glue only.
36	Autologous sheep fresh bone marrow mononuclear cells or BMSCs	Collagenase-induced Achilles tendon injury	Sheep	Fibrin glue	Nil	8 weeks	Both the fresh bone marrow mononuclear cell-fibrin glue group and the BMSC-fibrin glue group showed better histology, higher expression of collagen type I and COMP and lower expression of collagen type III compared to the fibrin glue-only group and saline-only group.
37	Autologous horse BMSCs	Collagenase-induced SDFT injury	Horse	PBS	+/- Overexpression of IGF-1	8 weeks	The histological score, immunohistochemical staining of collagen type I, of the healing tendons were better in the MSC and IGF-MSC groups compared to their paired PBS-only controls. The healing tendons in the BMSC group and IGF-BMSC group

							showed insignificant higher stiffness compared to their paired PBS-only controls. There was no difference in the ultrasound parameters, DNA content, GAG content, total collagen content, tendon catabolic and anabolic gene expression in the BMSC and IGF-BMSC groups compared to their paired PBS-only controls. Overexpression of IGF-1 in BMSCs did not produce additional benefits in tendon repair.
38	Autologous sheep or horse fresh bone marrow mononuclear cells or BMSCs	(1) Collagenase-induced Achilles tendon injury (2) Collagenase-induced SDFT injury (3) Naturally-occurring flexor tendons or the suspensory ligament injuries	(1) Sheep (2) Horse (3) Horse	Not mentioned	Nil	(1) 6 weeks (2) 21 weeks (3) Mean 48 weeks (Range 16-150 weeks)	(1) Results were not mentioned (2) Both the fresh bone marrow mononuclear cell group and the cultured BMSC group resulted in similar regeneration of tendon ECM in terms of type I/III collagen ratio, fiber orientation and COMP expression. (3) Injection of uncultured bone marrow mononuclear cells improved tendon healing as shown by ultrasonography. 60% of horses returned to races and the re-injury rate was 25%. All owners judged the treatment as good to excellent in term of athletic success.
39	Autologous horse fresh bone marrow mononuclear cells or BMSCs	Collagenase-induced SDFT injury	Horse	Not mentioned	Nil	21 weeks	The injection of fresh bone marrow mononuclear cells or the injection of BMSCs promoted tendon repair compared to the placebo group as shown by better ultrasound image, better histology, higher immunohistochemical staining of collagen type I and lower staining of collagen type III in the healing tendon.
40	Autologous horse BMSCs	Naturally-occurring SDFT injury	Horse	Autologous bone marrow supernatant	Nil	Some more than 1 year	The injection of BMSCs in bone marrow supernatant to the injured tendon reduced the re-jury rate, which compared favorably to the previous studies using conventional management.
41	Autologous horse	Naturally-occurring SDFT injury	Horse	Autologous bone marrow supernatant	Nil	6 months	The injection of BMSCs in bone marrow supernatant promoted tendon repair as shown by better histological scoring, lower cellularity, DNA content, vascularity, water

	BMSCs						content, GAG content and MMP-13 activity as well as lower structural stiffness of the healing tendons compared to the saline injection group.
42	Autologous horse BMSCs	Naturally-occurring SDFT injury	Horse	Autologous bone marrow supernatant	Nil	Min. 2 years after returning to full work	The injection of BMSCs in bone marrow supernatant reduced the re-injury rate compared to 2 published studies involving other treatments.
43	Autologous horse BMSCs	Naturally-occurring SDFT injury	Horse	Fresh autologous serum	Nil	At least 2 years	The injection of BMSCs in serum showed better early tendon healing compared to the un-injected group as shown by ultrasound imaging. Nine out of 11 horses with the injection of BMSCs in serum returned to racing with good or even optimal results in the previous category of competition in 9 to 12 months without any re-injuring event. However, the un-injected group showed tendon re-injury after a median of 7 months.
44	Autologous horse fresh autologous bone marrow mononuclear cells or BMSCs	Naturally-occurring SDFT injury	Horse	Fibrin glue	Nil	21 weeks	Both the fresh bone marrow mononuclear cell-fibrin glue group and the cultured BMSC-fibrin glue group showed comparable better ultrasound findings, fiber orientation, higher collagen type I and COMP expression but lower collagen type III expression compared to the saline-only group and fibrin glue-only group.
45	Autologous horse BMSCs	Naturally-occurring tendonitis and desmitis	Horse	Autologous PRP	Nil	24 weeks	The injection of BMSCs in PRP promoted better tendon repair compared to the pin firing group as shown by ultrasound imaging. Thirteen out of 18 horses in the BMSC group returned to race competition while none of the 12 horses returned to competition in the pin firing group.
46	Autologous horse BMSCs	Naturally-occurring SDFT injury	Horse	Bone marrow supernatant	Nil	until returned to full work	Eighteen percent of treated horses had re-injury, which compared favorably to conventional management reported in previous studies (56%).
47	Allogeneic	TBJ injury in Achilles	Rat	Fibrin glue	Nil	45 days	The BMSC-fibrin glue group showed higher healing rate, failure load and better

	rat BMSCs	tendon					organized enthesis compared to the natural repair group and the fresh chondrocyte-fibrin glue control group.
48	Allogeneic rat BMSCs	TBJ injury in Achilles tendon	Rat	DMEM	+/- Overexpression of CXCL13	8 weeks	Both the injection of BMSCs and BMSCs-overexpressing CXCL13 improved the biomechanical properties of the surgically repaired tendon compared to the injection of medium-only, with the injection of BMSCs-overexpressing CXCL13 showing the best outcome.
49	Autologous rat BMSCs	TBJ injury in supraspinatus tendon	Rat (inbred)	Fibrin glue	+/- Overexpression of Scx	4 weeks	The transplantation of Scx-BMSCs in fibrin glue showed more fibrocartilage at the insertion site; higher ultimate load, ultimate stress and stiffness compared to the transplantation of untreated BMSCs in fibrin glue.
50	Autologous rat BMSCs	TBJ injury in supraspinatus tendon	Rat (inbred)	Fibrin glue	+/- Overexpression of BMP-13	4 weeks	The transplantation of BMSCs overexpressing BMP-13 in fibrin glue did not improve rotator cuff healing compared to transplantation of non-transduced BMSCs in fibrin glue as shown by histomorphometric analysis and biomechanical test.
51	Autologous rat BMSCs	TBJ injury in supraspinatus tendon	Rat (inbred)	Fibrin glue	+/- Overexpression of MTI-MMP	4 weeks	The transplantation of BMSCs overexpressing MT1-MMP in fibrin glue promoted better TBJ healing by inducing more fibrocartilage formation at the insertion site and improving the biomechanical strength of the healing tissue compared to the transplantation of non-transduced BMSCs in fibrin glue.
52	Autologous rat BMSCs	TBJ injury in supraspinatus tendon	Rat (inbred)	Fibrin glue	Nil	4 weeks	The transplantation of BMSCs in fibrin glue did not improve new cartilage formation, collagen fiber organization and strength of TBJ compared to the fibrin glue-only group and natural healing group as shown by histology and biomechanical test.
53	Autologous rat BMSCs	TBJ injury in supraspinatus tendon	Rat (inbred)	Fibrin glue	+/- Downregulation of TGIF1	4 weeks	The transplantation of TGIF1 siRNA-BMSCs in fibrin glue promoted better tendon repair histologically with higher level of chondrogenic proteins and biomechanically compared to the transplantation of non-transduced BMSCs in fibrin glue
54	Autologous rat bone marrow-deriv	TBJ injury in supraspinatus tendon	Rat	Nil	Nil	8 weeks	Infiltration of bone marrow-derived cells after drilling of greater tuberosity increased the ultimate force-to-failure of the healing TBJ compared to the undrilled group.

	ed cells						
55	Autologous rabbit BMSCs	TBJ injury in infraspinatus tendon	Rabbit	PGA sheet	Nil	16 weeks	The transplantation of BMSCs seeded in PGA sheet promoted the regeneration of fibrocartilage zone and Sharpey's fiber formation, which were not observed in the PGA sheet-only group and natural healing group. More collagen type I compared to collagen type III were formed in the BMSC-PGA sheet group while more type III collagen compared to collagen type I were formed in the PGA sheet-only group. The BMSC-PGA sheet group showed higher tendon maturation score and tensile strength compared to the PGA sheet-only group and natural healing group.
56	Human BMSCs	Tendon-muscle junction injury in Achilles tendon	Rat	Polypropylene surgical mesh-PGA-alginate hydrogel	Nil	14 days	The transplantation of BMSC-loaded mesh enhanced quality of tendon-muscle junction repair as shown by histology and collagen type I expression compared to the mesh-only and suture repair.
57	Allogeneic circulating stem cells derived from a separate sponge wound model	Achilles tendon transfection	Rat	Nonwoven PGA	Nil	6 weeks	The transplantation of circulating stem cells seeded in PGA enhanced the biomechanical properties and histological score of the healing tendons compared to the PGA-only group.
58	Autologous sheep peripheral blood MSCs (PB-MSCs)	Collagenase-induced deep digital flexor tendon injury	Sheep	For the PB-MSC+PRP group: autologous PRP; For the PB-MSC group: Hyaluronic acid	Nil	120 days	The transplantation of PB-MSCs promoted tendon repair compared to the saline-injection group regarding tendon morphology and ECM composition but the addition of PRP did not enhance the regenerative response of PB-MSCs.
59	Autologous blood-derive	Naturally-occurring SDFT injury	Horse	PBS	Use the CD90+ cells	3 years	The injection of blood-derived stem cells promoted tendon repair as shown by ultrasound imaging at 4-5 months. There was no recurrence of tendon injury in the

	d stem cells						treated horse up to 3 years. The control horses treated with conventional therapy showed fibrotic scar tissue in ultrasound imaging and were re-injured within 3 to 6 months of recover.
60	C3H10T1/2 mouse multipotent cell line	Achilles tendon transection	Mouse	Nil	+/- Overxpression of Mkx followed by culturing the cells with ascorbic acid for 2 weeks to form the cell sheet	4 weeks	The Mkx-MSC group showed better histology, higher collagen deposition, larger fiber diameter and better biomechanical properties of the healing tendons compared to the eGFP-MSC control group.
61	C3H10T1/2 mouse multipotent cell line	Achilles tendon transection	Nude rat	Fibrin glue	+/- Overexpression of Egr1	3 weeks	Injection of Egr1-MSCs in fibrin glue promoted tendon repair as shown by histology, increase in tendon-related gene expression and collagen content compared to the injection of non-engineered MSCs in fibrin glue.
62	C3H10T1/2 mouse multipotent cell line	Achilles tendon segmental defect	Mouse	Fibrin glue	+/- Overexpression of Smad8 L+MH2/BMP2	3 weeks	The genetically engineered MSC-fibrin glue group showed significant higher stiffness and elastic modulus as well as better histology of the healing tendons compared to the non-engineered MSC-fibrin glue group which was similar to the fibrin glue-only group. The transplantation of non-engineered MSCs in fibrin glue did not improve the biomechanical properties of the healing tendons compared to the fibrin glue-only group.
63	C3H10T1/2 mouse multipotent cell line	Achilles tendon partial segmental defect	Nude rat	Collagen sponge	Overexpression of luciferase +/- Overexpression of Smad8 L+MH2/BMP2	7 weeks	The transplantation of MSCs overexpressing Smad8 L+MH2/BMP2, but not MSCs overexpressing Smad8 L+MH2 or MSC-overexpressing BMP2, induced tendon regeneration as shown by double quantum filtered MRI.

64	C3H10T1/2 mouse multipotent cell line	Achilles tendon segmental defect	Rat	Aligned or randomly-oriented PLLA scaffold	Nil	8 weeks	The transplantation of MSCs seeded on aligned electrospun scaffold form more mature tendon-like tissue compared to MSCs seed on randomly oriented scaffold as shown by better histology score, higher immunohistochemical staining of collagen type I, higher collagen content, higher mRNA expression of tendon-related markers, larger collagen fiber diameter and higher but insignificant biomechanical properties of the healing tendons. The aligned group formed less ectopic cartilage and bone compared to the random group.
65	Rabbit periosteal progenitor cells (PPCs) (not mentioned autologous or allogeneic)	TBJ injury in infraspinatus tendon	Rabbit	Injectable hydrogel (PEGDA containing photoinitiator plus BMP-2 tethered with PEG).	Nil	8 weeks	The PPCs-BMP-2-hydrogel group showed more fibrocartilage and bone at the TBJ and higher maximum pull-out load compared to the hydrogel-only group.
66	Autologous rabbit ADSCs	Achilles tendon transection	Rabbit	Not mentioned	Nil	28 days	The transplantation of ADSCs improved fiber structural organization and increased blood vessel formation in the healing tendons at day 14 compared to the transection-only group and the results were comparable to the suture group.
67	Allogeneic rat ADSCs	Achilles tendon transection	Rat	Tendon hydrogel +/- PRP	Nil	8 weeks	The transplantation of ADSCs, PRP or both in hydrogel augmented ultimate load and histology of the healing tendons compared to the transplantation of hydrogel alone. The transplantation of both ADCSs and PRP in hydrogel showed the best outcomes as shown by histology and ultimate load.
68	Autologous rabbit ADSCs	Achilles tendon transection	Rabbit	Autologous PRP	Nil	4 weeks	The transplantation of ADSCs in PRP increased the tensile strength, expression of collagen type I, FGF and VEGF as well as decreased the expression of TGF-β of the healing tendons compared to the PRP-only group

69	Autologous rabbit ADSCs	Achilles tendon partial segmental defect	Rabbit	Scaffold composed of an inner part of PGA unwoven fibers and an outer part of a net knitted PGA/PLA fibers	Tensile loading at 10% strain, 3 cycles/min, 1h/12 h for 5 weeks	45 weeks	The transplantation of ADSCs seeded in scaffold increased the collagen fibril diameter and tensile strength as well as improved the histological structure of the healing tendons compared to the scaffold-only group.
70	Allogeneic rabbit fresh adipose derived stromal vascular fraction	Deep digital flexor tendon transection	Rabbit	PBS	Nil	8 weeks	The injection of fresh adipose derived stromal vascular fraction to the injury site enhanced the biomechanical properties of the healing tissue compared to the PBS control group
71	Allogeneic rabbit fresh adipose derived stromal vascular fraction or BMSCs	Deep digital flexor tendon transection	Rabbit	PBS	Nil	8 weeks	Both the injection of fresh adipose derived stromal vascular fraction and BMSCs improved the biomechanical properties of the healing tendons compared to the PBS controls, with the injection of fresh adipose derived stromal vascular fraction showing better results.
72	Autologous horse ADSCs	Collagenase-induced SDFT injury	Horse	Autologous platelet concentrate	Nil	16 weeks	The injection of ADSC-platelet concentrate prevented lesion progression reduced the infiltration of inflammatory cells, improved collagen fiber organization and blood flow in the healing tendons compared to the injection of PBS. There was no difference in the mRNA expression of tendon-related markers between the two groups.

73	Autologous horse adipose-derived nucleated cells	Collagenase-induced SDFT injury	Horse	PBS	Nil	6 weeks	The adipose-derived nucleated cell group showed better histology and higher COMP mRNA expression compared to the PBS-only group. However, there was no difference in ultrasonographic parameters of tendon healing, content of DNA, proteoglycan and total collagen as well as gene expression of collagen type I and collagen type III between the two groups.
74	Human ADSCs	Collagenase-induced supraspinatus tendon injury	Rat	Saline	Nil	28 days	The injection of ADSCs reduced the infiltration of inflammatory cells, improved histology and biomechanical strength of the healing tendons at the early stage of tendon healing (first 2 weeks) compared to the saline control.
75	Allogeneic horse ADSCs	Naturally-occurring SDFT injury	Horse	Autologous PRP	Nil	24 months	After combined treatment with ADSCs and PRP, 89.5% horses returned to their previous level of competition while the re-injury rate was 10.5%. The results were comparable to the recent study with the transplantation of autologous BMSCs.
76	Allogeneic horse ADSCs	Naturally-occurring tendinitis	Horse	Activated autologous PRP	Nil	240 days	Fourteen out of sixteen horses recovered and returned to activity
77	Allogeneic rat ADSCs	TBJ injury in supraspinatus tendon	Rat	Collagen	Nil	4 weeks	The transplantation of ADSCs seeded in collagen did not improve the biomechanical properties and orientation of collagen fibers but showed less inflammation in the healing tendons compared to the collagen-only group.
78	Autologous rat ADSCs	TBJ injury in supraspinatus tendon	Rat	Fibrin glue	Nil	8 weeks	The transplantation of ADSCs in fibrin glue did not improve histological and biomechanical outcomes of TBJ healing compared to the injury-only and fibrin glue-only groups.
79	Allogeneic rabbit ADSCs	TBJ injury in subscapularis tendon	Rabbit	Hank's balanced salt solution	Nil	6 weeks	Both the injection of ADSC alone and saline alone without suture repair failed to heal the TBJ. The injection of ADSC with suture repair significantly improved muscle function, reduced fatty infiltration and insignificantly enhanced the load-to-failure of the TBJ compared to the injection of saline with suture repair.
80	Allogeneic rat Achilles	Achilles tendon transection	Rat	Collagen +/- activated PRP	Nil	3 weeks	Both TDSC-collagen and TDSC-PRP-collagen constructs stimulated tendon healing compared to the natural healing group, with TDSC-PRP-collagen constructs promoting

	TDSCs						better tendon repair compared to the TDSC-collagen constructs as shown by histology and biomechanical test.
81	Allogeneic rat Achilles TDSCs	Achilles tendon segmental defect	Rat	Collagen sponge +/- allogeneic PRP	Nil	2 weeks	TDSCs and PRP have synergistic effects on tendon healing under both loaded and unloaded conditions; and loaded conditions promoted better tendon healing as shown by higher mRNA and protein expression of tendon-related markers.
82	Allogeneic rabbit rotator cuff TDSCs	Rotator tendon segmental defect	Rabbit	Knitted silk-collagen sponge + collagen gel	Nil	12 weeks	The transplantation of TDSCs seeded in scaffold increased fibroblastic cell ingrowth and reduced the infiltration of lymphocytes. This group also showed better histological score, higher collagen deposition and better biomechanical properties compared to the scaffold-only group.
83	Human Achilles TDSCs	Achilles tendon window injury	Rat (immunosuppressed)	Porcine tendon-derived decellularized matrix	Nil	4 weeks	The transplantation of TDSCs seeded in decellularized matrix showed better histology, larger collagen fibrils, higher collagen deposition and stronger biomechanical properties of the healing tendon compared to the transplantation of decellularized matrix-only
84	Allogeneic rat patellar TDSCs	Patellar tendon window injury	Rat	+/- Rat skin fibroblasts-derived matrix sheet	Nil	8 weeks	The transplantation of TDSCs seeded in decellularized fibroblast matrix promoted better histological outcomes and biomechanical properties of the healing tissue compared to the injection of TDSCs alone.
85	Allogeneic rat patellar TDSCs	Patellar tendon window injury	Rat	Nil	Pretreatment with CTGF and ascorbic acid	8 weeks	The pre-treated TDSC group promoted better tendon repair compared to the injury-only group as shown by histology and biomechanical test.
86	Allogeneic rat patellar TDSCs	Patellar tendon window injury	Rat	Fibrin glue	+/- Overexpression of Scx	8 weeks	The transplantation of Scx-TDSCs in fibrin glue promoted tendon repair at the early stages (week 2 and week 4) compared to the transplantation of empty vector-TDSCs in fibrin glue and fibrin glue alone as shown by histology, biomechanical test and immunohistochemical staining of collagen type I. There was no difference in the degree of ectopic mineralization among different groups.
87	Allogeneic	Patellar tendon window	Rat	Fibrin glue	Nil	16 weeks	The transplantation of TDSCs in fibrin glue suppressed the infiltration of inflammatory

	rat patellar TDSCs	injury					cells and promoted tendon healing histologically with no increased risk of ectopic chondro-ossification compared to the transplantation of fibrin glue alone.
88	Allogeneic rat patellar TDSCs	Patellar tendon window injury	Rat	Fibrin glue	Nil	4 weeks	The transplantation of TDSCs in fibrin glue promoted earlier and better tendon repair as shown by histology and biomechanical test compared to the fibrin glue-only group.
89	Human patellar TDSCs	Patellar tendon core defect	Nude rat	+/- Rabbit extracellular tendon matrix or PBS	Nil	8 weeks	The transplantation of TDSCs with extracellular tendon matrix promoted better tendon repair as shown by the thicker and more organized collagen fibrils in histology compared to the transplantation of TDSCs alone.
90	Allogeneic rabbit patellar TDSCs	Patellar tendon window injury	Rabbit	PLCL/collagen	+/- Tensile loading at 4% strain, 0.5 Hz, 2h/day for 14 days	12 weeks	The loaded TDSC-scaffold group promoted better tendon repair as shown by better histology, higher immunohistochemical staining of tendon-related ECM proteins, collagen content and biomechanical properties of the healing tendons compared to the un-loaded TDSC-scaffold group which in turns was better than the scaffold-only group.
91	Allogeneic rat Achilles TDSCs	Collagenase-induced Achilles tendon injury	Rat	Saline +/- allogeneic PRP		8 weeks	The addition of TDSCs to PRP treatment enhanced the effects of PRP treatment alone as shown by better histological score, higher biomechanical properties, higher expression of tendon-related markers and lower expression of non-tenocyte markers in the healing tendons. However, TDSC injection alone had little effect on tendon healing compared to the saline control group.
92	Autologous rat TDSCs	TBJ injury in supraspinatus tendon	Rat (inbred)	Fibrin glue	+/- Transfection with TSG-6 siRNA	4 weeks	The transplantation of TDSCs in fibrin glue promoted TBJ repair compared to the transplantation of fibrin glue only as shown by biomechanical test. Silencing the expression of TSG-6 in TDSCs abrogated the benefits of TDSCs.
93	Allogeneic rabbit patellar TDSCs	TBJ injury in supraspinatus tendon	Rabbit	Fibrin glue	+/- Overexpression of Egr1	8 weeks	The transplantation of Egr1-TDSCs in fibrin glue enhanced tendon healing as shown by better histological score, more and better alignment of collagen fibers as well as more Sharpey's fibers at the TBJ compared to the transplantation of non-transduced TDSCs in fibrin glue which in turns was better than the repair-only group.
94	Allogeneic	Naturally-occurring injures	Horse	Reconstituted with	Conditioned	Up to 2 years	The re-injury rate was significantly lower and the lesional ecogenicity improved in the

	horse amniotic membrane-derived mesenchymal progenitor cells	of SDFT, suspensory ligament and collateral ligament of distal interphalangeal joint		sterile water	medium of amniotic membrane-derived mesenchymal progenitor cells was used for treatment.		conditioned medium-injection group compared to the un-injected control group.
95	Allogeneic horse amniotic membrane-derived mesenchymal progenitor cells	Naturally-occurring acute SDFT rupture/lesion and lesion of accessory ligament of the deep digital flexor tendon	Horse	Autologous plasma	Nil	90 days	The injection of amniotic membrane-derived mesenchymal progenitor cells in autologous plasma promoted tendon repair as shown by ultrasound imaging.
96	Allogeneic horse amniotic membrane-derived stem cells or autologous BMSCs	Naturally-occurring tendon and ligament injuries	Horse	Autologous plasma	Nil	2 years after return to full work	The injection of amniotic membrane-derived stem cells in plasma reduced the re-injury rate compared to the injection of autologous BMSCs in plasma.
97	Allogeneic sheep	Collagenase-induced Achilles tendon injuries	Sheep	Saline	Stable clones overexpressing	30 days	The injection of amniotic fluid-derived stem cell enhanced tendon repair compared to the saline-injection group as shown by better biomechanical properties, better

	amniotic fluid-derived stem cells				GFP		histology, stronger expression of collagen type I and null expression of collagen type III of the healing tendons.
98	Sheep amniotic epithelial mesenchymal cell	Naturally-occurring acute and chronic tendinopathy of SDFT	Horse	α MEM	Nil	180 days	Ultrasound and histological analyses showed improvement in tendon echotexture and histology after stem cell injection.
99	Allogeneic horse UCB-MSCs	Naturally-occurring tendinitis of SDFT, desmitis of suspensory ligament, tendinitis of deep digital flexor tendon and desmitis of inferior check ligament	Horse	Not mentioned	Nil	At least 6 months	77% of the horse returned to work on the same or higher level within 6 months after UCB-MSC injection.
100	Allogeneic horse UCB-MSCs	Naturally-occurring tendinopathy of SDFT	Horse	PBS	Nil	12 weeks	The UCB-MSC-treated horses recovered from their clinical condition and showed good ultrasound image of the healing SDFT.
101	Human ESC line or human fetal cells isolated from femur bone of fetuses	Achilles tendon segmental defect	Nude mouse	Nil	Differentiation to connective tissue progenitors (CTPs) followed by high-density culture up to 4 months to form a	6 months	The transplantation of fetal-derived CTPs or ESC-derived CTPs increased the leg extension angle > 90^{o} of transplanted mice and the mice ran significantly faster compared to the un-transplanted mice. There was an increase in stress in the tendon graft after *in-vivo* transplantation for 8 weeks

					cell sheet		
102	Human ESC line	Achilles tendon segmental defect	Rat (immunosuppressed)	Knitted silk-collagen sponge	Differentiation to MSCs and transfected with GFP	4 weeks	The ESC-MSC-scaffold group promoted better tendon repair as shown by better histological score, higher mRNA and protein expressions of tendon-related markers, collagen content and biomechanical properties of the healing tendons compared to the scaffold-only group.
103	Human ESC line	Achilles tendon segmental defect	Rat (immunosuppressed)	Knitted silk-collagen sponge	Differentiation to MSCs +/- overexpression of Scx	8 weeks	The transplantation of ESC-MSCs-Scx seeded in scaffold showed better tendon repair as shown by better histology, higher gene expression of tendon-related ECM proteins and better biomechanical properties compared to the transplantation non-transduced ESC-MSCs seeded in scaffold.
104	Human ESC line	Patellar tendon window injury	Rat (immunosuppressed)	Fibrin glue	Differentiation to MSCs	4 weeks	The ESC-MSCs-fibrin glue group has higher collagen content, better histology, larger collagen fibrils and better but insignificant biomechanical properties compared to the fibrin glue-only group. ESC-MSCs secreted human fetal tendon-specific matrix components and differentiation factors during the repair process.
105	Allogeneic horse fetal derived embryonic-like stem cell line (fdESC)	Collagenase gel-induced injury of SDFT	Horse	Eagle's essential medium	Nil	8 weeks	The fdESC group showed better tissue architecture, tendon size, lesion size and tendon linear fiber pattern as shown by ultrasound imaging and histology compared to the medium-only group. There was no difference in the tendon-related gene expression, total proteoglycan, collagen or DNA content at the repaired site between groups.
106	Human iPSCs	Achilles tendon segmental defect	Rat (immunosuppressed)	Well-aligned or random chitosan-based ultrafine fibers	Differentiation to MSCs	4 weeks	The seeding of iPSC-MSCs on well-aligned chitosan-based ultrafine fibers promoted better tendon repair compared to the seeding of iPSC-MSCs on random chitosan-based ultrafine fibers as shown by higher histological score, collagen content, ECM and tendon-related marker gene expression, immunohistochemical staining of collagen type I and decorin, collagen fiber diameters and biomechanical properties of the healing

							tendons
107	Human iPSCs	Patellar tendon window defect	Nude rat	Fibrin glue	Differentiation to neural crest stem cells (NCSCs)	4 weeks	The transplantation of iPSC-NCSCs in fibrin glue enhanced tendon repair compared to the fibrin glue-only control as shown by macroscopic, histological and biomechanical examinations. The transplanted iPSC-NCSCs increased the production of fetal tendon-related matrix proteins, stem cell recruitment factors, tenogenic differentiation factors and accelerated the host endogenous repair process.
108	Allogeneic human placenta-derived mesenchymal stromal cells	Refractory chronic Achilles tendinopathy	Human	Not mentioned	Nil	At least 4 weeks	No adverse events attributed to allogeneic MSC administration was noted in this phase I clinical trial with 6 patients.
109	Autologous human bone marrow mononuclear cells	Refractory chronic patellar tendinopathy	Human	Balanced solution	Nil	3-6 years (average 5 years)	There was significant improvement in the scores of Tegner scale, IKDC, KOOS symptoms, KOOS ADL, KOOS sport but not Lysholm, KOOS pain, KOOS QoL, SF-12-mental and SF-12-physical in the most recent follow-up in a series of 8 patients. The clinical scores improved up to 2 years and then plateaued up to 5 years. The ultrasound image improved at 6 months after inoculation.
110	Allogeneic human ADSCs	Chronic lateral epicondylosis	Human	Fibrin glue	Nil	1 year	There were no significant adverse effects of allogeneic ADSC injection in a series of 12 patients. The VAS score decreased, elbow performance score improved and ultrasound image of tendon defect improved.
111	Autologous human bone marrow concentrate	Full-thickness suprasupinatus tendon tear	Human	Nil	Nil	Minimum 10 years	The injection of bone marrow concentrate enhanced the healing rate and quality of arthroscopic repair compared to the control patients without bone marrow aspirate injection as shown by ultrasound imaging and MRI in this case-control study (45 patients in each group). Bone marrow concentrate injection also prevented further ruptures during the 10-year follow-up. Higher percentage of subjects have intact rotator

							cuff in the bone marrow concentrate injection group compared to the control group (87% versus 44%).
112	Autologous human bone marrow mononuclear cells	Full-thickness rotator cuff tear	Human	Saline with 10% autologous serum	Nil	At least 12 months	The transplantation of bone marrow mononuclear cells augmented conventional repair and increased the UCLA score (functional status) after 12 months in 14 patients. Clinical findings remained unaltered in all but one patient who relapsed into loss of strength and pain in the second year. MRI analysis showed tendon integrity in all cases after 12 months.

Footnote:

The PubMed database was searched with the key words “stem cells tendon” on 26-29 Jul 2015 and “bone marrow stromal cells tendon” on 17 Aug 2015 with no restriction in language and year of publication. The studies were selected after reviewing the titles and abstracts. The bibliographies of review articles were hand searched for further relevant articles. The search was limited to articles published in peer-reviewed journals. Only original articles were included. Single-case reports, reviews, letter to editors and experimental protocols were excluded. Only studies evaluating the safety and efficacy of stem cell application for the promoting TBJ repair of rotator cuff and Achilles tendon as well as tendon repair in animals and human were included. Studies on the safety and efficacy of stem cell application on tendon adhesion, ligament injuries and tendon healing within a bone tunnel in anterior cruciate ligament (ACL) reconstruction were excluded in this review due to space limitation. Studies examining the effects of stem cells after heterotopic transplantation in animals were excluded as these studies did not evaluate the effects of stem cell treatment on tendon repair directly. Studies evaluating the safety and efficacy of non-stem cell-based therapies such as the use of tenocytes, tendon fibroblasts or skin fibroblasts or tissue (such as periosteum and tendon grafts) were excluded. Studies that evaluated only the stem cell fate (such as cell viability) and mechanisms (such as inflammation and angiogenesis) after transplantation were also excluded.

Rows in grey are clinical studies.

Abbreviations:

ADL: Activities of daily living

ADSC: Adipose tissue-derived stem cell

bFGF: Fibroblast growth factor beta

ICAM-1: Intercellular cell adhesion molecule 1

IGF-1: Insulin-like growth factor 1

IKDC: International Knee Documentation Committee

PLCL: Poly(L-Lactide-co-ε-caprolactone

PLGA: Poly(lactic-co-glycolic acid)

PPCs: Periosteal progenitor cells

BMP: Bone morphogenetic protein-12

BMSC: Bone marrow-derived stem cell

COMP: Cartilage oligomeric matrix protein

CTGF: Connective tissue growth factor

CTPs: Connective tissue progenitors

CXCL13: Chemokine (C-X-C Motif) ligand 13

DMEM: Dulbecco's Modified Eagle Medium

DNA: Deoxyribonucleic acid

ECM: Extracellular matrix

eGFP: Enhanced green fluorescent protein

Egr1: Early growth response protein 1

ESC: Embryonic stem cell

fdESC: Fetal-derived embryonic stem cell

GAG: Glycoaminoglycan

GFP: Green fluorescent protein

iPSC: Induced pluripotent stem cell

KOOS: Knee Injury and Osteoarthritis Outcome Score

α-MEM: α-minimum essential medium

Mkx: Mohawk

MMP-13: Matrix metalloproteinase 13

MRI: Magnet resonance imaging

MSCs: Mesenchymal stem cell

MT1-MMP: Membrane type 1-matrix metalloproteinase 1

NCSC: Neural crest stem cell

PB-MSCs: Peripheral blood-mesenchymal stem cell

PBS: Phosphate buffered saline

PEG: poly(ethylene glycol)

PEGDA: Poly (ethylene glycol) diacrylate

PGA: Polyglycolic acid

PLA: Polylactic acid

PRP: Platelet-rich plasma

QoL: Quality of life

Scx: Scleraxis

SDFT: Superficial digital flexor tendon

Smad8: Mothers against decapentaplegic homolog 8

Smad8 L+MH2: Smad 8 linker + MH2 domain

TBJ: Tendon-bone junction

TDSC: Tendon-derived stem cell

TGF-β1: Transforming growth factor β1

TGIF1: 5'-TG-3'-interacting factor 1

TSG-6: TNF-stimulated gene 6 protein

UCB-MSCs: Umbilical cord blood-mesenchymal stem cells

UCLA: University of California, Los Angeles

VAS: Visual analog scale

VEGF165: Vascular endothelial growth factor 165

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