

**Table S2:** Specific search Strategy

1	Exosome* (Title OR Abstract OR Key words)
2	Extracellular vesicle* (Title OR Abstract OR Key words)
3	Exosomal (Title OR Abstract OR Key words)
4	Cell-Derived Microparticle* (Title OR Abstract OR Key words)
5	Secretome* (Title OR Abstract OR Key words)
6	Tendon* (Title OR Abstract OR Key words)
7	Ligament* (Title OR Abstract OR Key words)
8	Rotator cuff (Title OR Abstract OR Key words)
9	Achilles (Title OR Abstract OR Key words)
10	Enthesis (Title OR Abstract OR Key words)
11	Footprint (Title OR Abstract OR Key words)
12	Tendinous* (Title OR Abstract OR Key words)
13	Tendinopathy (Title OR Abstract OR Key words)
14	Tendinopathies (Title OR Abstract OR Key words)
15	Tendinosis (Title OR Abstract OR Key words)
16	Tendinitis (Title OR Abstract OR Key words)
17	1 OR 2 OR 3 OR 4 OR 5
18	6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16
19	17 AND 18

**Table S3:** Inclusion and Exclusion Criteria

	Inclusion Criteria	Exclusion Criteria
Study type	Original Article	Patent Conference Abstract Letter Case report Editorial and Editorial materials Review article
Language	English	Not English
Topic	Exosome and Tendon healing Exosome and Tendon-bone healing	Periodontal ligament or dental related diseases Not related to tendon OR tendon-bone healing Not related to Exosomes
Experiment type	In vivo or ex vivo experiment In vivo (ex vivo) and in vitro experiment	Only with in vitro experiment
Quality	Good quality of research studies	Poor quality of research

For articles which focus on the effect of extracellular vesicles promoting tendon, tendon-bone or ligament repair, we examined the distribution of extracellular vesicle diameters. Articles in which the distribution of diameters were significantly outside the distribution of exosomes (30~150nm) were excluded.

**Table S4:** Risk of bias assessed using SYRCLE risk of bias assessment tool

Author	Year	Selection bias			Performance bias		Detection bias		Attrition bias	Reporting bias	Other bias
		Sequence generation	Baseline characteristics	Allocation concealment	Random housing	Blinding	Random Outcome assessment	Blinding	Incomplete outcome data	Selective outcome reporting	Other sources of bias
Chamberlain et.al <sup>1</sup>	2019	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Chen et.al <sup>2</sup>	2021	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Cui et.al <sup>3</sup>	2019	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Davies et.al <sup>4</sup>	2022	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Fu et.al <sup>5</sup>	2021	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Gao et.al <sup>6</sup>	2022	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Gissi et.al <sup>7</sup>	2020	Unclear risk	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Han et.al <sup>8</sup>	2022	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Han et.al <sup>9</sup>	2022	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Hayashi et.al <sup>10</sup>	2022	Unclear risk	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Huang et.al <sup>11</sup>	2020	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Jenner et.al <sup>12</sup>	2023	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Li et.al <sup>13</sup>	2020	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Li et.al <sup>14</sup>	2022	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Li et.al <sup>15</sup>	2022	Unclear risk	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Liu et.al <sup>16</sup>	2021	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Liu et.al <sup>17</sup>	2021	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Ren	2021	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk

et.al <sup>18</sup>		r risk	risk	r risk	risk	risk					
Shen et.al <sup>19</sup>	2019	Unclea r risk	Low risk	Unclea r risk	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Shi et.al <sup>20</sup>	2020	Unclea r risk	Low risk	Unclea r risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Shi et.al <sup>21</sup>	2020	Unclea r risk	Low risk	Unclea r risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Song et.al <sup>22</sup>	2022	Unclea r risk	Low risk	Unclea r risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Tao et.al <sup>23</sup>	2021	Unclea r risk	Low risk	Unclea r risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Wang et.al <sup>24</sup>	2019	Unclea r risk	Low risk	Unclea r risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Wang et.al <sup>25</sup>	2019	Unclea r risk	Low risk	Unclea r risk	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Wang et.al <sup>26</sup>	2022	Unclea r risk	Low risk	Unclea r risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Wang et.al <sup>27</sup>	2021	Unclea r risk	Low risk	Unclea r risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Wang et.al <sup>28</sup>	2021	Unclea r risk	Low risk	Unclea r risk	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Wang et.al <sup>29</sup>	2020	Unclea r risk	Low risk	Unclea r risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Wellins et.al <sup>30</sup>	2021	Unclea r risk	Low risk	Unclea r risk	High risk	High risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Wu et.al <sup>31</sup>	2022	Unclea r risk	Low risk	Unclea r risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Wu et.al <sup>32</sup>	2021	Unclea r risk	Low risk	Unclea r risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Xu et.al <sup>33</sup>	2022	Unclea r risk	Low risk	Unclea r risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Xu et.al <sup>34</sup>	2023	Unclea r risk	Low risk	Unclea r risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Xu et.al <sup>35</sup>	2022	Unclea r risk	Low risk	Unclea r risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Yao et.al <sup>36</sup>	2020	Unclea r risk	Low risk	Unclea r risk	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Yao et.al <sup>37</sup>	2021	Unclea r risk	Low risk	Unclea r risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Ye et.al <sup>38</sup>	2023	Unclea r risk	Low risk	Unclea r risk	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Yu et.al <sup>39</sup>	2021	Unclea r risk	Low risk	Unclea r risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Yu et.al <sup>40</sup>	2020	Unclea r risk	Low risk	Unclea r risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Zhang et.al <sup>41</sup>	2022	Unclea r risk	Low risk	Unclea r risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk

Zhang et.al <sup>42</sup>	2022	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Zhang et.al <sup>43</sup>	2020	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Zhang et.al <sup>44</sup>	2022	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Zhao et.al <sup>45</sup>	2022	Unclear risk	Low risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Zhu et.al <sup>46</sup>	2022	Unclear risk	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk

**Table S5:** Summary of parameters of exosomes (Tendon healing and tendon-bone healing)

Author	Year	Origin/Source	Isolation method	Storage	Characterization	Size Distribution	EV/Exosome makers
Chamberlain et.al <sup>1</sup>	2019	Human BM-MSC exosomes	Differential centrifugation and ultracentrifugation	NR	NTA, FCM	61 ~ 121 nm	CD146, CD29, CD44, CD63, CD81, CD105
Chen et.al <sup>2</sup>	2021	Rabbit ASC exosomes	Differential centrifugation	-80°C	NTA, TEM, WB	99.4~233.4 nm	CD9, CD63
Cui et.al <sup>3</sup>	2019	Mouse BMDM exosomes	Centrifugation and ultracentrifugation	NR	NTA, TEM, WB	70~150 nm	CD9, CD63, TSG101, Alix
Davies et.al <sup>4</sup>	2022	Mouse FAP	Differential centrifugation and ultracentrifugation	4°C	NTA	NR	NR
Fu et.al <sup>5</sup>	2021	Human ASC exosomes	Differential centrifugation and ultracentrifugation	NR	NTA, TEM, WB	30 ~ 150 nm	CD9, HSP70, TSG101 +ve; Calnexin -ve
Gao et.al <sup>6</sup>	2022	Human IP-MSC exosomes	Differential centrifugation and ultracentrifugation	NR	NFA, TEM, WB	50 ~ 200 nm	CD9, CD63, TSG101 +ve; GM130 -ve
Gissi et.al <sup>7</sup>	2020	Rat BM-MSC exosomes	Differential centrifugation and ultracentrifugation	-80°C	AFM, CONAN, WB	30~200nm	Annexin XI, Annexin V, TSG101, CD29, TERT
Han et.al <sup>8</sup>	2022	HU-MSC exosomes	Differential centrifugation and ultracentrifugation	NR	TEM, Nano FCM software, WB	42~197 nm	CD9, TSG101, Alix +ve; Calnexin -ve
Han et.al <sup>9</sup>	2022	Rabbit BM-MSC exosomes	Exosomes were extracted by Total Exosome Isolation Reagent	NR	NTA, TEM, WB, FCM	100 ~ 200 nm	CD9, CD63, ALIX, Annexin V, TSG101 +ve; Calnexin -ve
Hayashi et.al <sup>10</sup>	2022	Human BM-MSC exosomes	Differential centrifugation and ultracentrifugation	NR	NTA, WB	P5 EVs: 148±7 nm P12 EVs: 158±10 nm	CD63, CD81, Flotilin-1
Huang et.al <sup>11</sup>	2020	Rat BM-MSC exosomes	Differential centrifugation and	-80°C	TEM, WB	30 ~ 150 nm	CD9, CD63, CD 81

			ultracentrifugation				
Jenner et.al. <sup>12</sup>	2023	HU-MSC exosomes	Ultracentrifugation	-80°C	NTA, TEM, FCM	~126.63 nm	CD9, CD29, CD63, CD81
Li et.al. <sup>14</sup>	2022	Rat BM-MSC exosomes	Differential centrifugation and ultracentrifugation	NR	NTA, TEM, WB	30 ~ 200 nm	CD9, HSP70, TSG101
Li et.al. <sup>15</sup>	2022	Rat BM-MSC exosomes	Differential centrifugation and ultracentrifugation	NR	NTA, TEM, WB	~ 100 nm	CD9, CD63, TSG101 +ve; Calnexin -ve
Li et.al. <sup>13</sup>	2020	HU-MSC exosomes	Differential centrifugation and ultracentrifugation	NR	NTA, TEM, WB	30 ~ 150 nm	CD9, CD63, TSG101, Alix +ve; Calnexin -ve
Liu et.al. <sup>16</sup>	2021	Rat ASC exosomes	Differential centrifugation and ultracentrifugation	NR	NTA, TEM, WB	~ 109.6 nm	CD9, TSG101, HSP70
Liu et.al. <sup>17</sup>	2021	Rat TSC	Differential centrifugation and ultracentrifugation	NR	NTA, TEM, WB	100~200 nm	CD9, CD63, TSG101
Ren et.al. <sup>18</sup>	2021	PEP	NA	-80°C	NTA, TEM	56.4~151 nm	NA
Shen et.al. <sup>19</sup>	2019	Mouse ASC exosomes	Differential centrifugation and ultracentrifugation	NR	TEM, NTA, WB	IEVs: 108±2 nm EVs: 113±3 nm	CD9, CD63
Shi et.al. <sup>20</sup>	2020	Mouse BM- MSC exosomes	Differential centrifugation and ultracentrifugation	-80°C	NTA, TEM, WB	~120.3 nm	CD9, CD81, TSG101
Shi et.al. <sup>21</sup>	2020	PEP	NA	NR	NTA, TEM	93.70~124.65 nm	NA
Song et.al. <sup>22</sup>	2022	Rat TSC exosomes	Differential centrifugation and ultracentrifugation	NR	NTA, TEM, WB	~139 nm	CD9, CD63, CD81, TSG101
Tao et.al. <sup>23</sup>	2021	Human TSPC exosomes	Differential centrifugation and ultracentrifugation	NR	TEM, DLS, WB	73.59±38.15 nm	CD9, CD63, CD81
Wang et.al. <sup>26</sup>	2022	Human ASC exosomes	Differential centrifugation and ultracentrifugation	NR	NR	NR	NR
Wang et.al. <sup>27</sup>	2021	Human ASC exosomes	Differential centrifugation and ultracentrifugation	NR	NR	NR	NR
Wang et.al. <sup>28</sup>	2021	Mouse BM- MSC exosomes	Differential centrifugation and ultracentrifugation	NR	NTA, TEM, WB	100~150 nm	Hsp70, CD9, CD63, CD81, TSG101
Wang et.al. <sup>29</sup>	2020	Human ASC exosomes	Differential centrifugation and ultracentrifugation	NR	TEM, NTA, WB	50~150 nm	CD9, CD63, TSG101 +ve; GM130 -ve
Wang et.al. <sup>24</sup>	2019	Human ASC exosomes	Differential centrifugation and ultracentrifugation	NR	TEM, NTA, WB	50~150 nm	CD9, CD63, TSG101 +ve; GM130 -ve

Wang et.al <sup>25</sup>	2019	Rat TSC exosomes	Differential centrifugation and ultracentrifugation	NR	TEM, WB	40~200 nm	CD63, CD81
Wellings et.al <sup>30</sup>	2021	PEP	NA	NR	NR	NR	NA
Wu et.al <sup>31</sup>	2022	Human BM-MSC exosomes	Differential centrifugation and ultracentrifugation	-80°C	NTA, TEM, WB	80 ~ 160 nm	Hsp70, CD9, CD81, TSG101 +ve; Calnexin -ve
Wu et.al <sup>32</sup>	2021	Rat BM-MSC exosomes	Differential centrifugation and ultracentrifugation	-80°C	NTA, TEM, WB	50~200 nm	CD9, CD63, TSG101 +ve; Calnexin -ve
Xu et.al <sup>33</sup>	2022	Rat ASC	Differential centrifugation and ultracentrifugation	-80°C	NTA, TEM, WB	Exosomes: 145.96±0.5 nm Ectosomes: 227.66±4.9 nm	CD9、CD63、TSG101、Hsp70、Alix +ve ; Calnexin -ve
Xu et.al <sup>34</sup>	2023	Human ASC exosomes	Differential centrifugation	-80°C	NTA, TEM, WB	EV <sub>N</sub> : 155.9±27.6 nm EV <sub>B</sub> : 146.8±15.2 nm	CD9, CD63 +ve; Calnexin -ve
Xu et.al <sup>35</sup>	2022	Rat IPFP-MSC exosomes	Differential centrifugation and ultracentrifugation	NR	NTA, TEM, WB	50 ~ 150 nm	CD63, CD81, TSG101
Yao et.al <sup>36</sup>	2020	HU-MSC exosomes	Differential centrifugation and ultracentrifugation	-80°C	NTA, TEM, WB	30 ~ 200 nm	CD9, CD63, Alix, TSG101
Yao et.al <sup>37</sup>	2021	HU-MSC exosomes	Differential centrifugation and ultracentrifugation	-80°C	NTA, TEM, WB	~137 nm	CD9, CD63, Alix
Ye et.al <sup>38</sup>	2023	Human IP-MSC exosomes	Differential centrifugation and ultracentrifugation	-80°C	NTA, TEM, WB	Small EVs: ~100 nm Large EVs: ~225 nm	CD9, CD63, TSG101 +ve; GM130 -ve
Yu et.al <sup>39</sup>	2021	Mouse BMDM exosomes	Centrifugation and ultracentrifugation	NR	TEM, WB	70~150 nm	CD63, CD81, TSG101
Yu et.al <sup>40</sup>	2020	Rat BM-MSC exosomes	Differential centrifugation and ultracentrifugation	-80°C	NTA, TEM, WB	50.5~151.7 nm	CD9, TSG101, Alix
Zhang et.al <sup>41</sup>	2022	Rabbit BM-MSC exosomes	Differential centrifugation and ultracentrifugation	NR	NTA, TEM, WB	50 ~ 150 nm	CD9, CD63, TSG101, Alix
Zhang et.al <sup>42</sup>	2022	Rat ASC exosomes	Differential centrifugation and ultracentrifugation	NR	NTA, TEM, WB	50~150 nm	CD9, CD63, TSG101
Zhang et.al <sup>43</sup>	2020	Rat TSC exosomes	Differential centrifugation and ultracentrifugation	NR	TEM, WB	~116 nm	CD9, TSG101, HSP70
Zhang et.al <sup>44</sup>	2022	Rat BM-MSC	Differential	NR	NTA, TEM, WB	50~100 nm	CD63, CD81, TSG101

		exosomes	centrifugation and ultracentrifugation				
Zhao et.al <sup>45</sup>	2022	Rat ASC exosomes	Differential centrifugation and ultracentrifugation	NR	TEM, DLS, WB	100~200 nm	CD9, CD63, TSG101
Zhu et.al <sup>46</sup>	2022	Human IP-MSC exosomes	Differential centrifugation and ultracentrifugation	-80°C	NFA, TEM, WB	60~160 nm	CD9, TSG101, CD63 +ve ; GM130 -ve

IP-MSC, induced pluripotent mesenchymal stem cells; NFA, Nano-flow analysis; TEM, Transmission electron microscope; WB, Western blot; BM-MSC, bone marrow mesenchymal stem cell; NR, not reported; P5 EVs, extracellular vesicles from mesenchymal stem cell at passage 5; P12 EVs, extracellular vesicles from mesenchymal stem cell at passage 12; NTA, nanoparticle tracking analysis; TSC, tendon stem cell; ASC, Adipose stem cell; IEVs, IFN  $\gamma$ -primed Extracellular vesicles; EVs, Extracellular vesicles; TSPC, tendon stem/progenitor cell; DLS, Dynamic Light Scattering; PEP, Purified Exosome Product; NA, not available; FAP, Fibroadipogenic progenitor; HU-MSC, Human umbilical cord mesenchymal stem cell; BMDMs, bone marrow-derived macrophages; AFM Atomic Force Microscopy; CONAN Colloidal Nano plasmonic assay; FCM, Flow Cytometry; EV<sub>B</sub>, bioactive glasses-elicited mesenchymal stem cell extracellular vesicle; EV<sub>N</sub>, native mesenchymal stem cell extracellular vesicle; IPFP MSC, Infrapatellar fat pad mesenchymal stem cell

**Table S6:** Summary of animal studies and treatment parameters. (Tendon healing)

Author	Year	Group/treatment	Concentration	Volume	Delivery route	Frequency	Euthanasia
Chamberlain et.al <sup>1</sup>	2019	(1) No treatment	NA	NA	NA	NA	1, 2 weeks
		(2) MSC	NR	NR	Local Injection	At day 0	1, 2 weeks
		(3) MQ	NR	NR	Local Injection	At day 0	1, 2 weeks
		(4) EEM	NR	NR	Local Injection	At day 0	1, 2 weeks
		(5) Exosomes	NR	NR	Local Injection	At day 0	1, 2 weeks
Chen et.al <sup>2</sup>	2021	(1) PBS	NA	NR	Local Injection	At day 0	4 weeks
		(2) Exosomes	NR	NR	Local Injection	At day 0	4 weeks
Cui et.al <sup>3</sup>	2019	(1) BDMD exosomes	NR	20 mg	Intravenous injection	Once every 3 days	3 weeks
		(2) Empty liposomes	NA	20 mg	Intravenous injection	Once every 3 days	3 weeks
Davies et.al <sup>4</sup>	2022	(1) PBS	NA	NR	Local Injection	At day 0	6 weeks
		(2) Exosomes from UCP1++ cells	2× 10 <sup>9</sup> particles	NR	Local Injection	At day 0	6 weeks
		(3) Exosomes from UCP1- cells	2× 10 <sup>9</sup> particles		Local Injection	At day 0	6 weeks
Fu et.al <sup>5</sup>	2021	(1) PBS	NA	100 $\mu$ L	Local Injection	At week 4	8, 12 weeks
		(2) Hydrogel	NA	100 $\mu$ L	Local Injection	At week 4	8, 12 weeks
		(3) Exosomes with hydrogel	0.3 mg/mL	100 $\mu$ L	Local Injection	At week 4	8, 12 weeks
		(4) No treatment	NA	NA	NA	NA	8, 12 weeks
Gao et.al <sup>6</sup>	2022	(1) Sham group	NA	NA	NA	NA	5 weeks
		(2) PBS	NA	NR	Local Injection	At week 1	5 weeks
		(3) Exosomes	1× 10 <sup>9</sup> particles/ml	NR	Local Injection	At week 1	5 weeks

Gissi et.al <sup>7</sup>	2020	(1) PBS	NA 4× 10 <sup>6</sup>	50 µL	Local Injection	At day 0	30 days
		(2) Rat BM-MSC with PBS	particles/50 µL 2.8× 10 <sup>12</sup>	50 µL	Local Injection	At day 0	30 days
		(3) EV <sub>L</sub> with PBS	particles/mL 8.4× 10 <sup>12</sup>	50 µL	Local Injection	At day 0	30 days
		(4) EV <sub>H</sub> with PBS	particles/mL	50 µL	Local Injection	At day 0	30 days
Han et.al <sup>8</sup>	2022	(1) No treatment	NA	NA	NA	NA	1 week
		(2) Sham group	NA	NA	NA	NA	1 week
		(3) Exosomes	100 µg/50 µL	50 µL	Subcutaneous injection	At day 0	1 week
Hayashi et.al <sup>10</sup>	2022	(1) P5 EVs with PBS	3595±480 ng/20 µL	20 µL	Local Injection	At day 1 and day 7	1, 4 weeks
		(2) P12 EVs with PBS	3655±626 ng/20 µL	20 µL	Local Injection	At day 1 and day 7	1, 4 weeks
		(3) PBS	NA	20 µL	Local Injection	At day 1 and day 7	1, 4 weeks
Jenner et.al <sup>12</sup>	2023	(1) Ringer lactate solution and collagen sponge	NA 2× 10 <sup>10</sup>	100 µL	Implantation	At day 0	6 weeks
		(2) Exosomes with ringer lactate solution and collagen sponge	particles in 100 µL	100 µL	Implantation	At day 0	6 weeks
Li et.al <sup>14</sup>	2022	(1) Fibrin sealant	NA	30 µL	Local Injection	At day 0	1, 2, 8 weeks
		(2) TSCs with fibrin sealant	5× 10 <sup>4</sup> particles in	30 µL	Local Injection	At day 0	1, 2, 8 weeks
		(3) BM-MSC-EV treated TSCs with fibrin sealant	30 µL 5×	30 µL	Local Injection	At day 0	1, 2, 8 weeks
		(4) EUG-BM-MSC-EV treated TSCs with fibrin sealant	10 <sup>4</sup> particles in 30 µL 5× 10 <sup>4</sup> particles in 30 µL	30 µL	Local Injection	At day 0	1, 2, 8 weeks
Li et.al <sup>13</sup>	2020	(1) PBS	NA	50 µL	Subcutaneous injection	At day 0	3 weeks
		(2) Exosomes	200 µg/50 µL	50 µL	Subcutaneous injection	At day 0	3 weeks
		(3) HCPT-exosomes	200 µg/50 µL	50 µL	Subcutaneous injection Subcutaneous injection	At day 0	3 weeks
Liu et.al <sup>16</sup>	2021	(1) Sham group	NA	NA	NA	NA	1, 2, 4 weeks
		(2) GelMA	NA	30 µL	Implantation	At day 0	1, 2, 4 weeks
		(3) Exosomes with GelMA	200 µg/30 µL	30 µL	Implantation	At day 0	1, 2, 4 weeks

Liu et.al <sup>17</sup>	2021	(1)	No treatment	NA	NA	NA	NA	4 weeks
		(2)	Sham group	NA	NA	NA	NA	4 weeks
		(3)	Exosomes	NR	NR	Local Injection	At week 2	4 weeks
		(4)	Exosomes/MBA	NR	NR	Transdermal delivery	At week 2	4 weeks
Shen et.al <sup>19</sup>	2019	(1)	Collagen sheet	NA	5 mm <sup>3</sup>	Implantation	At day 0	7 days
		(2)	Collagen sheet loaded with EVs	5~6× 10 <sup>9</sup> particles/sheet	5 mm <sup>3</sup>	Implantation	At day 0	7 days
		(3)	Collagen sheet loaded with IEVs	5~6× 10 <sup>9</sup> particles/sheet	5 mm <sup>3</sup>	Implantation	At day 0	7 days
Shi et.al <sup>21</sup>	2020	(1)	No treatment	NA	NA	NA	NA	4 weeks
		(2)	Tisseel patch	NA	NR	Implantation	At day 0	4 weeks
		(3)	PEP with Tisseel patch	1× 10 <sup>12</sup> particles/ml	NR	Implantation	At day 0	4 weeks
Song et.al <sup>22</sup>	2022	(1)	Sham group	NA	NA	NA	NA	2, 4, 8 weeks
		(2)	PHA	NA	200μL	Local Injection	At day 0	2, 4, 8 weeks
		(3)	Exosomes with PHA	2 × 10 <sup>10</sup> particles/200 μL	200 μL	Local Injection	At day 0	2, 4, 8 weeks
Tao et.al <sup>23</sup>	2021	(1)	Sham group	NA	NA	NA	NA	4 weeks
		(2)	Hydrogel	1× 10 <sup>11</sup> particles/ml	0.1 cm <sup>3</sup>	Implantation	At day 0	4 weeks
		(3)	Con-EVs with hydrogel	1× 10 <sup>11</sup> particles/ml	0.1 cm <sup>3</sup>	Implantation	At day 0	4 weeks
		(4)	H19-sOE-EVs with hydrogel	1× 10 <sup>11</sup> particles/ml	0.1 cm <sup>3</sup>	Implantation	At day 0	4 weeks
		(5)	hnRNP A2/B1-EVs with hydrogel	1× 10 <sup>11</sup> particles/ml	0.1 cm <sup>3</sup>	Implantation	At day 0	4 weeks
		(6)	H19-OL-EVs with hydrogel	1× 10 <sup>11</sup> particles/ml	0.1 cm <sup>3</sup>	Implantation	At day 0	4 weeks
Wang et.al <sup>26</sup>	2022	(1)	No treatment	NA	NA	NA	NA	6, 12 weeks
		(2)	Fibrin	NA	NR	Local Injection	At day 0	6, 12 weeks
		(3)	Exosomes with fibrin	1× 10 <sup>11</sup> particles/mL	NR	Local Injection	At day 0	6, 12 weeks
		(4)	Sham group	NA	NA	NA	NA	12 weeks
Wang et.al <sup>27</sup>	2021	(1)	Saline	NA	10 μL	Injection around the enthesis site	At week 6	10 weeks
		(2)	Exosomes with saline	1× 10 <sup>11</sup> particles in	10 μL	Injection around the enthesis site	At week 6	10 weeks
		(3)	Saline	10 μL NA	10 μL	Injection around the enthesis site	At week 6	10 weeks

Wang et.al. <sup>24</sup>	2019	(1)	Sham group	NA	NA	NA	NA	8, 16 weeks
		(2)	Saline	NA	20 $\mu$ L	Local Injection	At day 0	8, 16 weeks
		(3)	Exosomes with saline	$1 \times 10^{11}$ particles/20 $\mu$ L	20 $\mu$ L	Local Injection	At day 0	8, 16 weeks
Wang et.al. <sup>25</sup>	2019	(1)	No treatment	NA	NA	NA	NA	5 weeks
		(2)	Rat TSCs	$1 \times 10^6$ particles in	20 $\mu$ L	Local Injection	Twice a week	5 weeks
		(3)	Exosomes from rat TSCs	20 $\mu$ L 0.486 $\mu$ g/ $\mu$ L	20 $\mu$ L	Local Injection	Twice a week	5 weeks
Wellings et.al. <sup>30</sup>	2021	(1)	Sham group	NA	NA	NA	NA	3, 6 weeks
		(2)	Type 1 collagen scaffold	NA	NR	Apply at the repair site	At day 0	3, 6 weeks
		(3)	PEP with type 1 collagen scaffold	$1 \times 10^{11}$ particles/ml	NR	Apply at the repair site	At day 0	3, 6 weeks
Xu et.al. <sup>33</sup>	2022	(1)	Saline	NA $1 \times 10^{10}$ particles in	25 $\mu$ L	Local Injection	At week 1	3, 5 weeks
		(2)	Exosomes	25 $\mu$ L	25 $\mu$ L	Local Injection	At week 1	3, 5 weeks
		(3)	Ectosomes	$1 \times 10^{10}$ particles in 25 $\mu$ L	25 $\mu$ L	Local Injection	At week 1	3, 5 weeks
Xu et.al. <sup>34</sup>	2023	(1)	Intact, no treatment	NA	NA	NA	NA	3 days, 1, 2, 4 weeks
		(2)	Surgery, no treatment	NA	NA	NA	NA	3 days, 1, 2, 4 weeks
		(3)	GelMA hydrogel	NA	20 $\mu$ L	Implantation	At day 0	3 days, 1, 2, 4 weeks
		(4)	EV <sub>B</sub> with GelMA hydrogel	80 $\mu$ g/20 $\mu$ L	20 $\mu$ L	Implantation	At day 0	3 days, 1, 2, 4 weeks
		(5)	EV <sub>N</sub> with GelMA hydrogel	80 $\mu$ g/20 $\mu$ L	20 $\mu$ L	Implantation	At day 0	3 days, 1, 2, 4 weeks
Yao et.al. <sup>36</sup>	2020	(1)	Sham group	NA	NA	NA	NA	3 weeks
		(2)	Exosomes with PBS	200 $\mu$ g/50 $\mu$ L	50 $\mu$ L	Subcutaneous injection	At day 0	3 weeks
		(3)	PBS	NA	50 $\mu$ L	Subcutaneous injection	At day 0	3 weeks
Yao et.al. <sup>37</sup>	2021	(1)	Sham group	NA	NA	NA	NA	2, 4 weeks
		(2)	Fibrin glue	NA	50 $\mu$ L	Implantation	At day 0	2, 4 weeks
		(3)	Fibrin glue with HU-MSC exosomes	100 $\mu$ g/50 $\mu$ L	50 $\mu$ L	Implantation	At day 0	2, 4 weeks
		(4)	Sham group	NA	NA	NA	NA	4 weeks
		(5)	Fibrin glue with agomir-NC exosomes	100 $\mu$ g/50 $\mu$ L	50 $\mu$ L, 100 $\mu$ g	Implantation	At day 0	4 weeks
		(6)	Fibrin glue with agomir-29a exosomes	100 $\mu$ g/50 $\mu$ L	50 $\mu$ L, 100 $\mu$ g	Implantation	At day 0	4 weeks

Ye et.al. <sup>38</sup>	2023	(1) Sham group	NA	NA	NA	NA	2, 4 weeks
		(2) PBS	NA	100 $\mu$ L	Local injection	At day 0	2, 4 weeks
		(3) Small EVs	$1 \times 10^{10}$ particles/ml	100 $\mu$ L	Local injection	At day 0	2, 4 weeks
		(4) Large EVs	$1 \times 10^9$ particles/ml	100 $\mu$ L	Local injection	At day 0	2, 4 weeks
Yu et.al. <sup>39</sup>	2021	(1) No treatment	NA	NA	NA	NA	2, 3 weeks
		(2) Sham group	NA	NA	NA	NA	2, 3 weeks
		(3) M2 macrophage exosomes	NR	NR	NR	At day 0	2, 3 weeks
		(4) CircRNA-Ep-400 depletion of M2 macrophage exosomes	NR	NR	NR	At day 0	2, 3 weeks
Yu et.al. <sup>40</sup>	2020	(1) Exosomes with fibrin	2 $\mu$ g/ $\mu$ L	10 $\mu$ L	Local Injection	At day 0	3 days, 1, 2, 4 weeks
		(2) PBS with fibrin	NA	10 $\mu$ L	Local Injection	At day 0	3 days, 1, 2, 4 weeks
Zhang et.al. <sup>41</sup>	2022	(1) Sham group	NA	NA	NA	NA	16, 20, 24 weeks
		(2) Fiber-aligned patch	NA	1 $cm^2$ (size of the patch)	Fix the patch on supraspinatus	At week 12	16, 20, 24 weeks
		(3) Exosomes-loaded fiber-aligned patch	NR	1 $cm^2$ (size of the patch)	Fix the patch on supraspinatus	At week 12	16, 20, 24 weeks
Zhang et.al. <sup>42</sup>	2022	(1) Saline	0.1 mg/kg	NR	Local Injection	At week 6	7 weeks
		(2) Dexamethasone	0.1 mg/kg	NR	Local Injection	At week 6	7 weeks
		(3) Exosomes with dexamethasone	$1 \times 10^{11}$ Particles/mL	NR	Local Injection	At week 6	7 weeks
Zhang et.al. <sup>43</sup>	2020	(1) GelMA with Exosomes from TSCs	200 $\mu$ g/30 $\mu$ L	30 $\mu$ L	Local Injection	At day 0	1, 2, 8 weeks
		(2) GelMA group	NA	30 $\mu$ L	Local Injection	At day 0	1, 2, 8 weeks
		(3) No treatment	NA	NA	NA	NA	1, 2, 8 weeks
Zhao et.al. <sup>45</sup>	2022	(1) Saline	NA	NR	Local Injection	At week 1	5 weeks
		(2) ASC with saline	$1 \times 10^6$ particles	NR	Local Injection	At week 1	5 weeks
		(3) Exosomes with saline	50 $\mu$ g	NR	Local Injection	At week 1	5 weeks
Zhu et.al. <sup>46</sup>	2022	(1) Sham tendinopathy group	NA	NA	NA	NA	8 weeks
		(2) PBS group	NA	100 $\mu$ L	Local Injection	weekly	8 weeks
		(3) PBS with Exosomes from IP-MSC	$1 \times 10^{10}$ particles in 100 $\mu$ L	100 $\mu$ L	Local Injection	Weekly	8 weeks
		(4)	$\mu$ L				
		(5) Steroid-treated group	NA	100 $\mu$ L	Local Injection	weekly	8 weeks

PBS, phosphate-buffered saline; IP-MSC, induced pluripotent mesenchymal stem cells; NA, not available; P5 EVs, extracellular vesicles from

mesenchymal stem cell at passage 5; P12 EVs, extracellular vesicles from mesenchymal stem cell at passage 12; GelMA, gelatin methacryloyl; TSCs, tendon stem cells; EVs, Extracellular vesicles; IEVs, IFN  $\gamma$ -primed Extracellular vesicles; Con-EVs, control extracellular vesicles; H19-sOE-EVs, extracellular vesicles derived from tendon stem/progenitor cells over-expressing H19; hnRNP A2/B1-EVs, extracellular vesicles derived from tendon stem/progenitor cells over-expressing hnRNP A2/B1; H19-OL-EVs, extracellular vesicles derived from tendon stem/progenitor cells co-overexpressed of H19 and hnRNP A2/B1; NR, not reported; PEP, purified exosome product; Exosomes/MBA, exosomes modified by a nitric oxide nanomotor; UCP1++ cells, Fibroadipogenic progenitors exhibiting a high UCP1 fluorescent intensity  $> 10^4$ , UCP1- cells, Fibroadipogenic progenitors that were UCP1-negative were defined as TdTomato fluorescent intensity  $< 10^2$ ; HU-MSC, Human umbilical cord mesenchymal stem cell; BMDM, bone marrow-derived macrophages; BM-MSCs, bone marrow mesenchymal stem cells; EV<sub>L</sub>, low concentration of Extracellular vesicles; EV<sub>H</sub>, high concentration of Extracellular vesicles; HCPT-exosomes, exosomes derived from human umbilical cord mesenchymal stem cell treated with hydroxycamptothecin; MSC, mesenchymal stem cells; MQ, macrophage; EEM, exosome-educated macrophages; PHA, photopolymerizable hyaluronic acid; BM-MSC-EV, bone marrow mesenchymal stem cells extracellular vesicle; EUG-BM-MSC-EV, eugenol treated bone marrow mesenchymal stem cells extracellular vesicle; EV<sub>B</sub>, bioactive glasses-elicited mesenchymal stem cell extracellular vesicle; EV<sub>N</sub>, native mesenchymal stem cell extracellular vesicle; ASC, Adipose stem cell

**Table S7:** Summary of animal studies and treatment parameters (Tendon-bone healing)

Author	Year	Group/treatment	Concentration	Volume	Delivery route	Frequency	Euthanasia
Han et.al <sup>9</sup>	2022	(1) Sham group	NA	NA	NA	NA	12 weeks
		(2) Exosomes	NR	NR	Injection into the key bone interface	At day 0	12 weeks
		(3) Exosomes with empty microcapsules	NR	NR	Injection into the key bone interface	At day 0	12 weeks
		(4) Exosomes with BMP-2-loaded microcapsules	NR	NR	Injection into the key bone interface	At day 0	12 weeks
Huang et.al <sup>11</sup>	2020	(1) PBS	NA	200 $\mu$ L	Injection into the tail vein	At week 4	8, 12 weeks
		(2) Exosomes with PBS	200 $\mu$ g/200 $\mu$ L	200 $\mu$ L	Injection into the tail vein	At week 4	8, 12 weeks
Li et.al <sup>15</sup>	2022	(1) PBS	NA	50 $\mu$ L	Injection into the joint cavity	At day 0, day 3, day 7	4, 8 weeks
		(2) BM-MSC Exosomes	$1 \times 10^{11}$ Particles/mL	50 $\mu$ L	Injection into the joint cavity	At day 0, day 3, day 7	4, 8 weeks
		(3) miR-23a-3p overexpression BM-MSC exosomes	$1 \times 10^{11}$ Particles/mL	50 $\mu$ L	Injection into the joint cavity	At day 0, day 3, day 7	4, 8 weeks
Ren et.al <sup>18</sup>	2021	(1) No treatment	NA	NA	NA	NA	6 weeks
		(2) Fibrin sealant	NA	27mm <sup>3</sup>	Implantation	At day 0	6 weeks
		(3) Exosomes with fibrin sealant	20% (vol/vol)	27mm <sup>3</sup>	Implantation	At day 0	6 weeks
Shi et.al <sup>20</sup>	2020	(1) Control group	NA	NR	Local Injection	At day 0	7, 14, 30 days
		(2) Hydrogel	NR	NR	Local Injection	At day 0	7, 14, 30 days
		(3) Exosomes with hydrogel	NR	NR	Local Injection	At day 0	7, 14, 30 days

Wang et.al <sup>28</sup>	2021	(1)	Control group	NA	NR	Injected into bone tunnels	At day 0	NR
		(2)	BM-MSC exosomes	1× 10 <sup>10</sup> Particles/leg	NR	Injected into bone tunnels	At day 0	NR
		(3)	BM – MSC <sup>AD</sup> exosomes	1× 10 <sup>10</sup> Particles/leg	NR	Injected into bone tunnels	At day 0	NR
		(4)	BM – MSC <sup>SCX</sup> exosomes	1× 10 <sup>10</sup> Particles/leg	NR	Injected into bone tunnels	At day 0	NR
						Injected into bone tunnels		
Wang et.al <sup>29</sup>	2020	(1)	Sham group 1	NA	NA	NA	NA	6 weeks
		(2)	Sham group 2	NA	NA	NA	NA	18 weeks
		(3)	No treatment	NA	NA	NA	NA	6 weeks
		(4)	Saline	NA	20μL/per side	Local Injection	At week 6	18 weeks
		(5)	Exosomes with saline	1× 10 <sup>11</sup> Particles/20 μL	20μL/per side	Local Injection	At week 6	18 weeks
Wu et.al <sup>31</sup>	2022	(1)	PBS	NA	NR	Local injection	At day 0	2, 4, 8 weeks
		(2)	Exosomes	100μg/tunnel	NR	Local injection	At day 0	2, 4, 8 weeks
		(3)	IONP-exosomes	100μg/tunnel	NR	Local injection	At day 0	2, 4, 8 weeks
Wu et.al <sup>32</sup>	2021	(1)	Saline	NA	20 μL	Local Injection	At day 0	2, 4 weeks
		(2)	BM-MSC exosomes	1× 10 <sup>11</sup> Particles/20μL	20 μL	Local Injection	At day 0	2, 4 weeks
		(3)	LIPUS-BM-MSC exosomes	1× 10 <sup>11</sup> Particles/20μL	20 μL	Local Injection	At day 0	2, 4 weeks
Xu et.al <sup>35</sup>	2022	(1)	No treatment	NA	NA	NA	NA	2, 4, 8 weeks
		(2)	PBS and SAH	NA	Intra-tunnel: 0.1 mL;Intra-articular: 0.2 mL	Intra-tunnel injection (SAH) and intra-articular injection (PBS)	Intra-tunnel injection: at day 0 intra-articular injection:	2, 4, 8 weeks
		(3)	IME and IME-loaded SAH	1× 10 <sup>10</sup> Particles/mL	Intra-tunnel: 0.1 mL;Intra-articular: 0.2 mL	Intra-tunnel injection (IME-loaded SAH) and intra-articular injection (IME)	injection: weekly Intra-tunnel injection: at day 0 intra-articular injection: weekly	2, 4, 8 weeks

Zhang et.al <sup>44</sup>	(1)	PBS	NA	300 μL	Injection into bone tunnels at 12, 4, and 8 o'clock directions	At day 0	2, 4, 8 weeks
2022	(2)	Normal exosomes with adhesive hydrogel	10 mg/mL	300 μL	Injection into bone tunnels at 12, 4, and 8 o'clock directions	At day 0	2, 4, 8 weeks
	(3)	Hypo-exosomes with adhesive hydrogel	10 mg/mL	300 μL	Injection into bone tunnels at 12, 4, and 8 o'clock directions	At day 0	2, 4, 8 weeks

PBS, phosphate-buffered saline; NA, not available; NR, not reported; BM-MSC, bone marrow mesenchymal stem cell; BM – MSC<sup>SCX</sup>, Scleraxis-overexpressing bone marrow mesenchymal stem cell; BM – MSC<sup>AD</sup>, bone marrow mesenchymal stem cell transfected with empty vectors; SAH, sodium alginate hydrogel; IME, infrapatellar fat pad mesenchymal stem cell-derived exosome; Hypo-exosomes, exosomes secreted by hypoxia-stimulated bone-marrow mesenchymal stem cells; IONP-exosomes, Exosomes derived from magnetically actuated bone marrow mesenchymal stem cells; BMP, Bone morphogenetic protein; LIPUS-BM-MSC, Bone Marrow Mesenchymal Stem Cell Preconditioned by Low-Intensity Pulsed Ultrasound Stimulation;

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