Supplement Table 2: Characteristics of animal models (A) exosomes isolation (B), characterization of cell surface proteins of administered exosomes (C), and sources of exosomes (D).

A: Overall characteristics of the studies

Study Model		EV Source		Injury Type		Outcome	
Mouse	32	MSC	22	Excision	40	Wound closure rate	43
Rat	19	Umbilical	8	Burn	23	Angiogenesis	24
Human	2	Plasma	3	Flap	3	Collagen deposition	7
Other	3	Other	18	Other models	4	Other	13

B: Isolation techniques used in the studies

Isolation Procedure	Mice	Rats	Total	%
Ultracentrifugation	19	16	35	70
Manufacturer's kit	8	0	8	16
Ultracentrifugation + Filtration	3	2	5	10
Tangential Flow & others	2	0	2	4

C: Percentage of studies utilizing different membrane surface proteins to visualize and characterize exosomes

CD markers	Mice	Rats	Total	% of studies
CD63	22	12	34	47.22
CD9	16	13	29	40.28
CD81	15	10	25	34.72
TSG101	11	4	15	20.83
HSP70	3	3	6	8.33
GM130	1	2	3	4.17
$Grp94^{-}$	1	1	2	2.78
Flotilin	1	1	2	2.78
Annexin V	1	1	2	2.78
Others (EpCam, GRP90. CD90, CD105, MHC-I, MHC-II, CD86)		1	1	1.39

D: Unique sources of biological materials used to isolate exosomes			
Sources of exosomes	Mice	Rats	Total studies
MSCs	14	8	22
Umbilical	3	5	8
Embryonic stem cells	2	-	2
Human PRP and Plasma	2	1	3
Fibroblast	2	1	3
HUVECs	2	2	4
Macrophage	-	1	1
Keratinocyte	1	1	2
Macrophage	-	1	1
Urine	1	-	1
DC cells	1	-	1
Others	4	1	5

Supplement Table 3: Isolation and Characterization of exosomes used in the study mice (a) and rats (b).

a. MICE STUDIES

	Authors	Animal Model	Sources of exosomes	Isolation techniques	Visualization techniques	Characterizations markers
1.	Xiong Y, et al. (Xiong Y. et al., 2020a)	C57BL/6	Plasma	Others	Microscopy, WB	CD81 and TSG101
2.	Liu K, et al. (Liu et al., 2019)	Nude	human liposuction	Ultracentrifugation	Microscopy	Not Stated
3.	Kobayashi H, et al. (Kobayashi et al., 2018)	C57BL/6S/J-Leprdb (db/db) mice	iPS cell culture media	MagCapture Exosome Isolation commercial Kit PS	Microscopy and Flow cytometry	CD9, CD63, and CD81
4.	He X, et al. (He et al., 2019)	C57BL/6	MSCs	Centrifugation and ExoQuick-TC commercial kit	Microscopy, WB	CD63 and CD81
5.	Su D, et al. (Su et al., 2020)	C57BL/6	Hu and mouse melanoma cell lines	Ultracentrifugation	Western, microscopy	CD63, CD81, Alix
6.	Zhang J, et al. (Xu et al., 2020)	C57BL/6	Endothelial progenitor cells	Centrifugation (10000g) with a gradient	Imaging, TEM, WB	CD9 and CD63
7.	Zhao G, et al. (Zhao G. et al., 2020)	C57BL/6	MSCs	Ultracentrifugation	WB, Microscopy	CD9 and CD63, TSG101, HSP70
8.	Wang L, et al. (Wang L. et al., 2019)	Mice (BALB/c)	huMSC	Ultracentrifugation	NanoSight, WB	CD9, CD63, and CD81
9.	Kim H, et al. (Kim et al., 2019)	Balb/c Mice	Mice BMSCs induced to either M1 or M2 Macrophage	Ultracentrifugation	TEM	CD63 and Alix

10.	Chen J, et al. (Chen Jialin et al., 2019)	Others	Others	Commercial Kit		TSG101, CD63, glycosylated CD63
11.	Zhao B, et al. (Zhao et al., 2018)	C57BL/6	hu Amnion	Ultracentrifugation	Flow cytometry, WB, Microscopy	CD9, CD63, and CD81
12.	Chen CY, et al. (Chen et al., 2018)	C57BL/6	urine-derived stem cells (USCs)	Centrifugation, filtration and Commercial Kit	Flow cytometry, WB, Microscopy	CD63 and TSG101
13.	Wang C, et al. (Shi Yu et al., 2019)	ICR	AMSCs-derived exosomes	ultracentrifugation	Flow cytometry, WB, Microscopy	Alix, CD63, CD9, CD81
14.	Wang M, et al. (Wang M. et al., 2019)	ICR		Ultracentrifugation	Flow cytometry, WB, Microscopy	CD9, CD29, CD44, CD81, SCA-1
15.	Trinh NT, et al. (Trinh et al., 2016)	Female C57BL/6	hu- ASC	Ultracentrifugation	Flow cytometry	CD105, CD90, and APC-anti-CD45
16.	Wang X, et al. (Wang Xiao et al., 2019)	C57BL/6	mouse full-thickness skin wound model	ExoQuick-TC commercial kit	WB, Microscopy	CD63, Alix, and Tsg101
17.	Xiong Y, et al. (Xiong Y. et al., 2020b)	C57BL/6	Peripheral blood of non-diabetic and diabetic patients with a foot wound	Ultracentrifugation	WB, Microscopy	CD9 and TSG101
18.	Zhang Y, et al. (Zhang et al., 2020)	C57BL/6	Female ASCs	Ultracentrifugation	WB, Microscopy, TEM	CD9, CD63
19.	Chen B, et al. (Chen Bi et al., 2019)	C57BL/6 and HUVEC cells	hESCs; H9	Ultracentrifugation	NanoSight, TEM, WB	CD9, CD63, TSG-101

20.	Hu Y, et al. (Hu et al., 2018)	HUVEC cells, fibroblasts, and 12 wks. male C57BL6 mice (26-30 g)	Human umbilical cord blood plasma (UCB-Exos)	Ultracentrifugation	Dynamic light scattering, TEM, Flow cytometry	CD63, TSG101
21.	Wang L, et al. (Wang et al., 2017)	Balb/c mice (6–8 wk. old). Full-thickness dorsal wounds (2.0 × 1.5 cm2)	SC adipose tissue from healthy mothers (18–30 years old) undergoing cesarean section	Ultra-15 Centrifugal Filter Device (Millipore) and ExoQuick-TC commercial Kit	NanoSight	CD63, CD9
22.	Yang C, et al. (Yang et al., 2020)	HaCaT cells. spontaneously transformed aneuploid immortal keratinocyte cell line from adult human skin), in vivo: BALb/c mouse	adipose tissue from a 2-year female patient from the abandoned tissue of full-layer skin transplant surgery	Ultracentrifugation	TEM, Flow cytometry, WB	CD63 and CD81
23.	Bakhtyar N, et al. (Bakhtyar et al., 2018)	mice excision model	Wharton's jelly of the human umbilical cord	Ultracentrifugation	TEM, SEM. Mass spectrophotometry to characterize exosome cargo.	CD81
24.	Hu L, et al. (Hu et al., 2016)	Adult male Balb/c mice	ASCs	ExoQuick-TC exosome commercial kit	Dynamic tracking video capture, WB, NanoSight	CD9 and CD63
25.	Dalirfardouei R, et al. (Dalirfardouei et al., 2019)	C57BL/6 (induced diabetic)	human volunteers-Menstrual Blood MSC	Ultracentrifugation	Field- emission scanning electron microscopy (MIRA3 TESCAN) and atomic force microscopy, WB	CD81, TSG101
26.	Geiger A, et al. (Geiger et al., 2015)	B6.Lept db/db (genetically diabetic)	Healthy human volunteers circulating fibrocytes	Ultracentrifugation	NanoSight, Flow cytometry, WB	CD9, CD63, CD81, MHC-I, MHC-II, CD80, CD86, TSG101, GM130,

						Flotillin-1
27.	Hu S, et al. (Hu et al., 2019)	Mouse Foxn1nu (nude mouse)	1. hBM-MSC 2. Human dermal fibroblasts 3. Human dermal fibroblasts	Ultracentrifugation / Ultrafiltration	NanoSight	CD81) and multivesicular body synthesis proteins (Alix)
28.	Yang K, et al. (Yang et al., 2019)	Mice (BALB/c)	hucMSC	QIAGEN exoEasy Maxi commercial kit	TEM, WB	HSP70, CD9
29.	Yin H, et al. (Yin et al., 2019)	Female C57BL/6	Cyanobacteria *Synechococcus elongatus* PCC7942	Ultracentrifugation and ultrafiltration	TEM, Nanosizer™ instrument	NA
30.	Li B, et al. (Li et al., 2020)	C57BL/6	mice BMSC	Ultracentrifugation	Flow cytometry, TEM, WB	CD63, CD81, TSG101, heat shock protein 70 (HSP70), and the negative marker GRP94 expression in exosomes
31.	Qiu X, et al. (Qiu et al., 2020)	C57BL/6	mice BMSC	Ultracentrifugation	WB, TEM	CD9, CD63, CD81 and TSG101
32.	Zhang Y, et al. (Zhang et al., 2019)	C57BL/6	ESC	Ultracentrifugation	WB, Microscopy	CD9, CD63

b. RATS STUDIES

	Authors	**Animal Model**	**Sources of exosomes**	**Isolation techniques**	**Visualization techniques**	**Characterization markers**
1.	Li M, et al. (Li et al., 2019)	Sprague Dawley	RAW 264.7 cells	Ultracentrifugation	Flow cytometry, TEM, WB	CD63 and Alix
2.	Zeng T, et al. (Zeng et al., 2019)	Sprague Dawley	HUVECs	Ultracentrifugation	NanoSight, laser light scattering spectrometer, TEM, WB	CD63, CD9, TSG101, Grp94
3.	Li X, et al. (Li Xiao et al., 2016)	Sprague Dawley	Human Umbilical Cord MSCs	Ultracentrifugation	NanoSight, laser light scattering spectrometer,	CD9 and CD63

					TEM, WB	
4.	Zhang J, et al. (Zhang J. et al., 2015)	Sprague Dawley	hiPSC-MSC	Ultracentrifugation	TEM, WB	CD9, CD63 and CD81
5.	Gao S, et al. (Gao et al., 2020)	Sprague Dawley	human amniotic MSCs (hAMSC)	Centrifugation and Filtration	TEM, WB, Particle Size	CD9, CD63 and CD81
6.	Zhang B, et al. (Zhang B. et al., 2015a)	Sprague Dawley	human Umbilical Cord MSCs (hucMSC)	Centrifugation and Filtration	TEM, Particle Size	CD9, CD63, and CD81
7.	Xiong J, et al. (Xiong J. et al., 2020)	Sprague Dawley	human ADSCs & human Foreskin Fibroblasts (HFF)	Ultracentrifugation	WB, TEM, Particle size	CD63, CD81, TSG101, and HSP70
8.	Guo SC, et al. (Guo et al., 2017)	Sprague Dawley	human PRP	Ultracentrifugation	WB, TEM, Particle size	CD9, CD63, CD81
9.	Zhang J, et al. (Zhang et al., 2016)	Sprague Dawley	human Umbilical cord MSC	Ultracentrifugation	TEM and Particle size	CD9, CD63, CD81
10.	Zhang B, et al. (Zhang B. et al., 2015b)	Male Albino Wistar rats	hucMSCs and HFL1 cell lines	Ultracentrifugation	Particle size, Microscopy, and WB	CD9, CD63, CD81 HSP70
11.	Zhao D, et al. (Zhao D. et al., 2020)	Sprague Dawley	HUVECs	Ultracentrifugation	Particle size, Microscopy, and WB	CD9, CD63, CD81, and HSP 70
12.	Ding J, et al. (Ding et al., 2019)	Sprague Dawley	BMSCs reconditioned by deferoxamine (DFO-Exos) to induce angiogenesis	Ultracentrifugation	TEM, NanoSight, WB	CD9, CD 63, TSG101, GM130
13.	Ismail DI, et al. (Ismail and Aboulkhair, 2018)	Sprague-Dawley	Rats' sub Q adipose tissue	Ultracentrifugation	intravenous injection of 200µ PKH26-labeled exosomes, imaging	not stated
14.	Jiang T, et al. (Jiang et al., 2020)	Sprague Dawley	hBM-MSC-Ex	Ultracentrifugation	Reported in the previous study via WB, TEM, NanoSight	not stated

15.	Li M, et al. (Li M. et al., 2016)	Male albino rats	human synovial MSCs (SMSC); overexpressing miR-126-3p	Ultracentrifugation	Particle Size, TEM	could not find the paper
16.	Liu J, et al. (Liu et al., 2020)	Sprague Dawley	hu Umbilical Cord MSCs (hucMSC	Ultracentrifugation	Particle Size, TEM, NTA	CD9, CD63, and CD81
17.	Lv Q, et al. (Lv et al., 2020)	Sprague Dawley	hu ASCs	Ultracentrifugation	Particle Size, TEM	CD9, CD 63, TSG101, CD81. GM130
18.	Sjöqvist S, et al. (Sjoqvist et al., 2019)	Sprague Dawley	human oral mucosal epithelial cells	Ultracentrifugation	Particle Size, TEM, WB	CD9, Flotilin+, Annexin V-, EpCAM, HSP70-, GRP90- (cell signaling)
19.	Shi R, et al. (Shi et al., 2020)	Sprague Dawley	ASCs derived exosomes	Not reported or the wrong reference provided	Not reported or the wrong reference provided	Not reported or the wrong reference provided

Supplement Table 1: Quality check of pre-clinical studies using modified STAIR guidelines.

MICE STUDIES												
Study #	Authors Name	Sample Size Calculation	Temperature Control	Publication in a Peer-Reviewed Journal	Treatment Randomization	Allocation Concealment	Avoidance of Anesthetics with Intrinsic Wound Healing Properties	Use of Animals with Relevant Comorbidities	Reporting of Animals Excluded from the Analysis	Statement of Compliance with Animal Welfare Regulations	Conflict of Interest	Sum
1	Xiong Y, et al. (Xiong Y. et al., 2020a)	0	0	1	1	0	1	1	0	1	1	6
2	Liu K, et al. (Liu et al., 2019)	0	0	1	1	0	1	0	0	0	1	4
3	Kobayashi H, et al. (Kobayashi et al., 2018)	0	1	1	1	1	0	1	0	1	1	7
4	He X, et al. (He et al., 2019)	0	0	1	1	0	1	0	0	1	1	5
5	Su D, et al. (Su et al., 2020)	0	0	1	1	0	1	0	0	1	1	5
6	Xu J, et al. (Xu et al., 2020)	0	0	1	0	0	1	0	0	1	1	4
7	Zhao G, et al. (Zhao G. et al., 2020)	0	1	1	1	0	1	0	0	1	1	6
8	Wang L, et al. (Wang L. et al., 2019)	0	0	1	0	0	1	0	0	1	1	4
9	Kim H, et al. (Kim et al., 2019)	0	0	1	1	0	1	0	0	1	1	5
10	Chen J, et al. (Chen Jialin et al., 2019)	0	0	1	0	0	1	0	0	1	1	4
11	Zhao B, et al. (Zhao et al., 2018)	0	1	1	1	0	1	0	0	1	1	6
12	Chen CY, et al. (Chen et al., 2018)	0	0	1	1	0	1	1	0	1	1	6

13	Shi, Y, et al. (Shi Yu et al., 2019)	0	0	1	0	0	1	1	0	1	1	5
14	Wang M, et al. (Wang M. et al., 2019)	0	0	1	1	0	1	1	0	1	1	6
15	Trinh NT, et al. (Trinh et al., 2016)	0	0	1	0	0	1	0	0	1	1	4
16	Wang X, et al. (Wang Xiao et al., 2019)	0	0	1	0	0	1	0	0	1	1	4
17	Xiong Y, et al. (Xiong Y. et al., 2020b)	0	0	1	1	0	1	0	0	1	1	5
18	Zhang Y, et al. (Zhang et al., 2020)	0	0	1	1	0	1	0	0	1	1	5
19	Chen, B, et al. (Chen Bi et al., 2019)	0	0	1	0	0	1	0	0	1	1	4
20	Hu Y, et al. (Hu et al., 2018)	0	0	1	1	0	1	0	0	1	1	5
21	Wang L, et al. (Wang et al., 2017)	0	0	1	1	0	1	0	0	1	1	5
22	Yang C, et al. (Yang et al., 2020)	0	0	1	0	0	1	0	0	1	1	4
23	Bakhtyar N, et al. (Bakhtyar et al., 2018)	0	0	1	1	0	1	0	0	1	1	5
24	Hu L, et al. (Hu et al., 2016)	0	0	1	1	0	1	0	0	1	1	5
25	Dalirfardouei R, et al. (Dalirfardouei et al., 2019)	0	1	1	1	0	1	0	0	1	1	6
26	Geiger A, et al. (Geiger et al., 2015)	0	1	1	1	0	1	0	0	1	0	5

27	Hu S, et al. (Hu et al., 2019)	0	0	1	1	0	1	0	0	1	1	5
28	Yang K, et al. (Yang et al., 2019)	0	1	1	1	0	1	0	0	1	1	6
29	Yin H, et al. (Yin et al., 2019)	0	0	1	1	0	1	0	0	1	1	5
30	Li B, et al. (Li et al., 2020)	0	0	1	1	0	1	1	0	1	1	6
31	Qiu X, et al. (Qiu et al., 2020)	0	1	1	0	0	1	0	0	1	1	5
32	Zhang Y, et al. (Zhang et al., 2019)	0	0	1	1	0	1	0	0	1	1	5
RAT STUDIES												
1	Li M, et al. (Li et al., 2019)	0	0	1	0	0	1	0	0	1	1	4
2	Zeng T, et al. (Zeng et al., 2019)	0	0	1	1	0	1	0	0	1	1	5
3	Li X, et al. (Li Xiao et al., 2016)	0	0	1	1	0	1	0	0	1	1	5
4	Zhang J, et al. (Zhang J. et al., 2015)	0	0	1	1	0	1	0	0	1	1	5
5	Gao S, et al. (Gao et al., 2020)	0	0	1	1	0	1	0	0	1	1	5
6	Zhang B, et al. (Zhang B. et al., 2015a)	0	1	1	1	0	1	0	0	1	1	6
7	Xiong J, et al. (Xiong J. et al., 2020)	0	0	1	1	0	1	0	0	1	1	5
8	Guo SC, et al. (Guo et al., 2017)	0	0	1	1	0	1	0	0	1	1	5
9	Zhang J, et al. (Zhang et al., 2016)	0	0	1	1	0	1	0	0	1	1	5

10	Zhang B, et al. (Zhang B. et al., 2015b)	0	1	1	1	0	1	0	0	1	1	6
11	Zhao D, et al. (Zhao D. et al., 2020)	0	0	1	1	0	1	0	0	1	1	5
12	Ding, J, et al. (Ding et al., 2019)	0	0	1	1	0	1	1	0	1	1	6
13	Ismail DI, et al. (Ismail and Aboulkhair, 2018)	0	1	1	1	0	1	0	0	1	1	6
14	Jiang, T, et al. (Jiang et al., 2020)	0	0	1	1	0	1	0	0	1	1	5
15	Li M, et al. (Li M. et al., 2016)	0	0	1	1	0	1	0	0	1	0	4
16	Liu J, et al. (Liu et al., 2020)	0	1	1	1	0	1	0	0	1	1	6
17	Lv Q, et al. (Lv et al., 2020)	0	0	1	1	0	1	0	0	1	1	5
18	Sjöqvist S, et al. (Sjoqvist et al., 2019)	0	0	1	1	0	1	0	0	1	0	4
19	Shi R, et al. (Shi et al., 2020)	0	0	1	1	0	1	0	0	1	1	5
Average		0	11	51	41	1	50	7	0	50	48	5.08
											Std	0.751597