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Supplementary Materials for

Knockdown of deleterious miRNA in progenitor cell-derived small extracellular vesicles enhances tissue repair in myocardial infarction

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This PDF file includes:

Figs. S1 to S6
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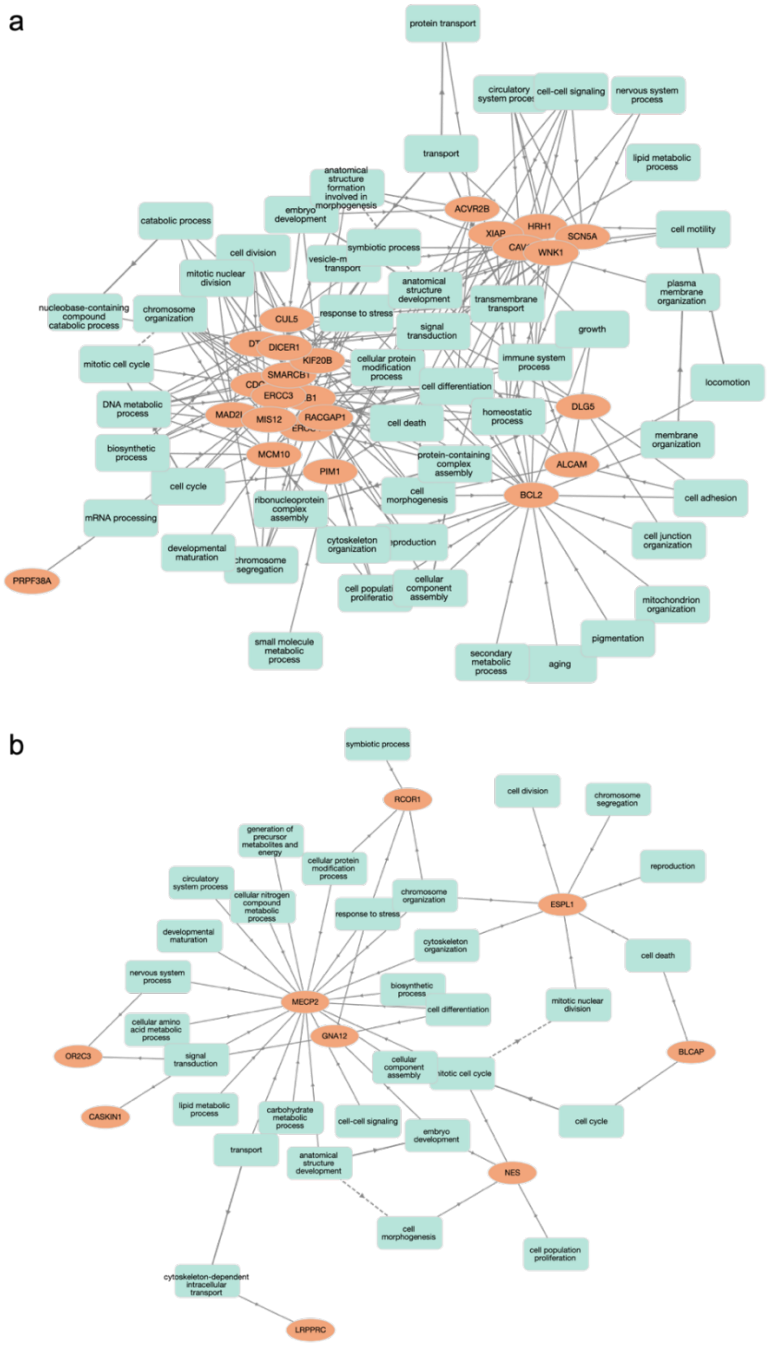
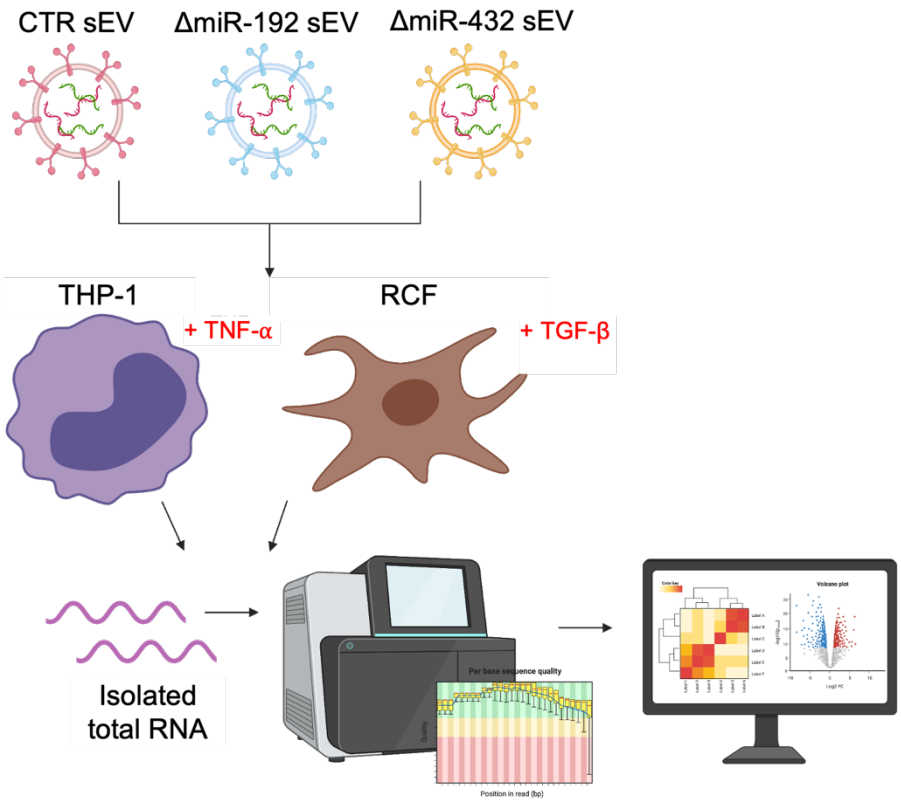
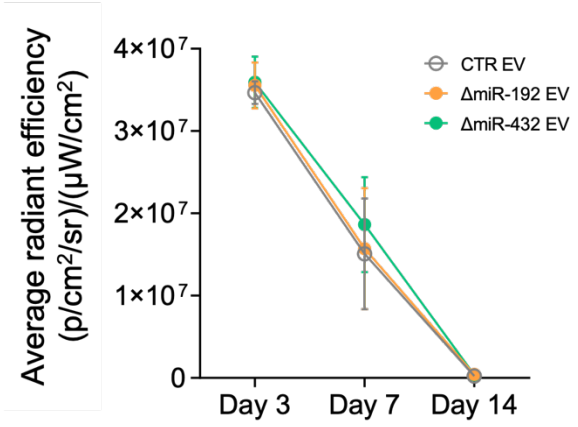


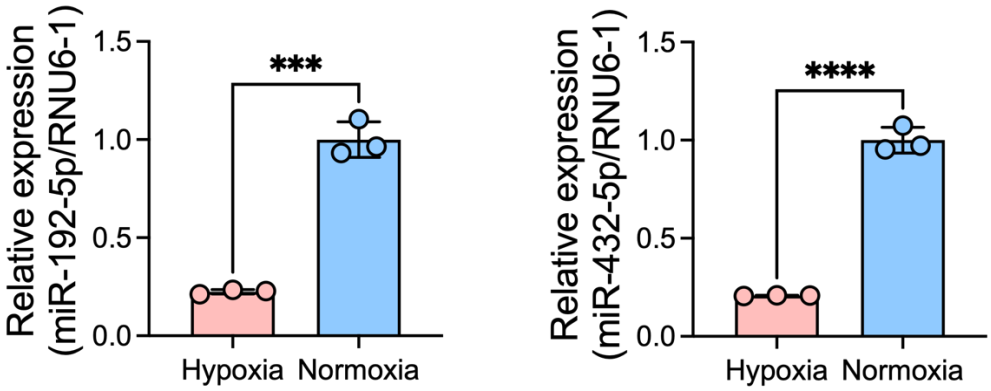
Supplementary Fig. S1. Interactive target gene annotation analyses of GO biological processes showed the connections between miRNA gene targets and biological processes. a, 25 targets of miR-192-5p and **b,** 9 targets of miR-432-5p that are validated with more than three assays. Interactive maps of target gene-GO terms were generated from GOnet web-based tool for interactive Gene Ontology analysis (https://tools.dice-database.org)[45].



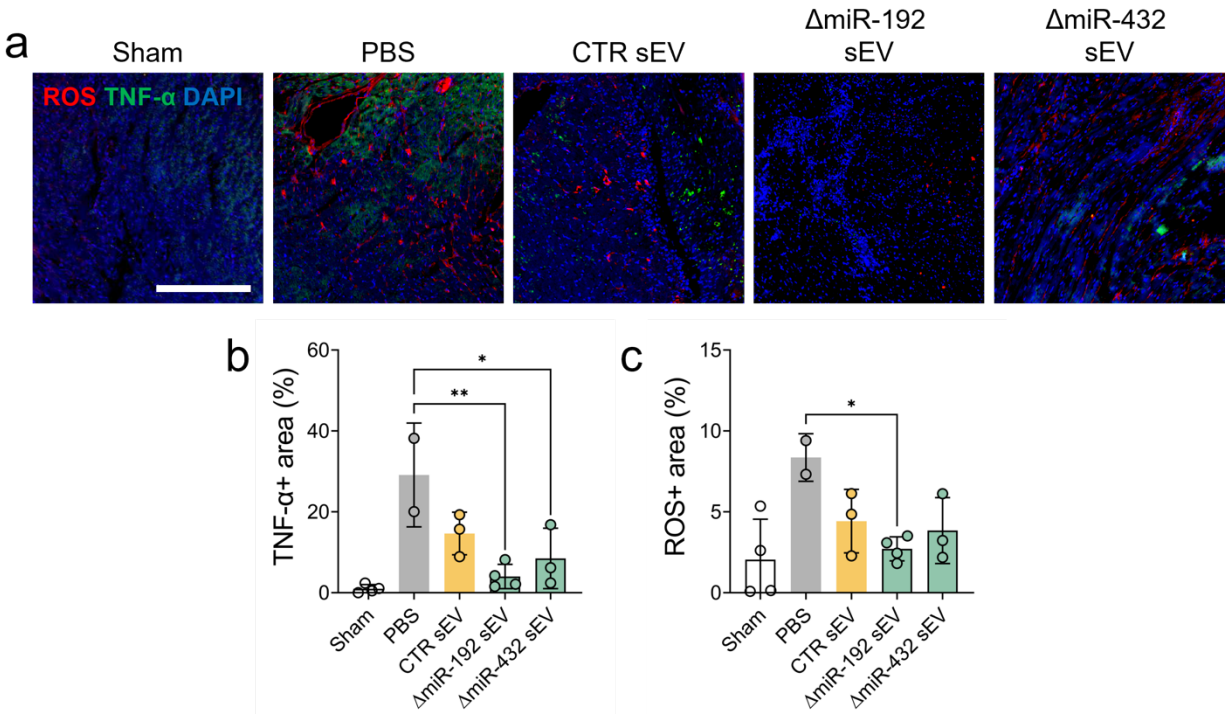
Supplementary Fig. S2. Schematic illustrations showed the process of recipient cells (THP-1 and RCF) RNA sequencing after various sEV treatment.



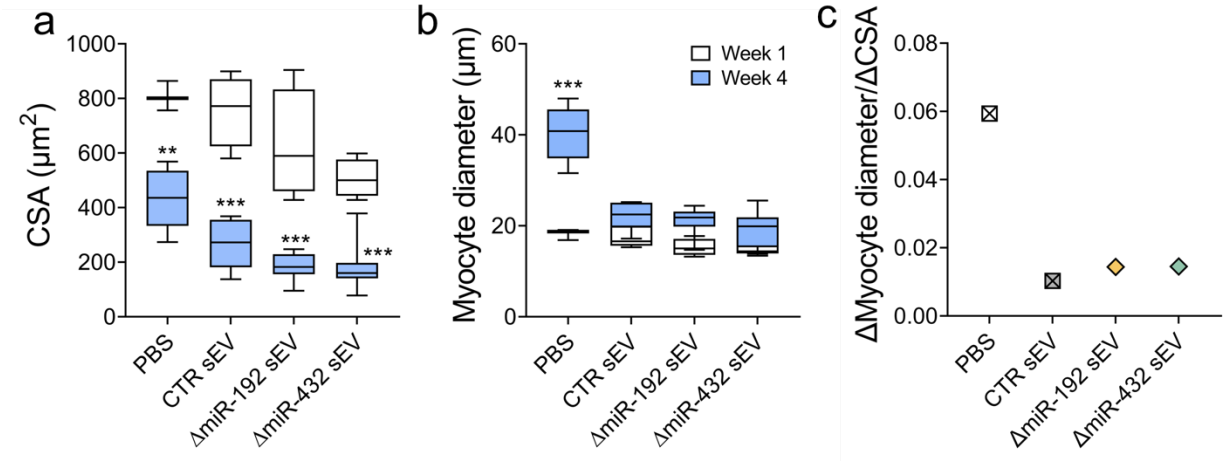
Supplementary Fig. S3. Time-course analysis determined the average radiant efficiency of sEVs in the heart 3-, 7-, and 14-days post sEV injection (n=4).



Supplementary Fig. S4. Relative miRNA expressions in CPC sEVs. CPCs were cultured under different oxygen concentration for 24 hours before serum depletion. sEVs were collected after 24 hours of serum depletion. ***$p<0.001$ and ****$p<0.0001$.



Supplementary Fig. S5. sEV administration showed anti-inflammatory responses in cardiac IR rats 7 days post-treatment. a, Immunohistochemical staining of ischemic hearts to detect TNF-α (green) and ROS (red) expressions. Scale bar indicates 200 µm. **b,** TNF-α positive area and **c,** ROS positive area measured from stained images. *$p<0.05$ and **$p<0.01$.



Supplementary Fig. S6. Morphological changes of myoblasts were observed in cardiac IR rats 1- and 4-weeks post treatment. a, CSA and **b,** myocyte diameter changes between week 1 and week 4 measured from WGA-stained images. **p<0.01 and ***p<0.001. **c,** Average ratio of changes of myocyte diameter and changes of CSA between week 1 and week 4.

Supplementary Table S1. 50 VIP miRNAs with high relativity with angiogenesis, fibrosis, and left ventricular EF in cardiac IR rat after exosome therapy.

Agarwal et al. (Ref 20)				Trac et al. (Ref 21)			
1	hsa-miR-874-3p	26	hsa-miR-23a-3p	1	hsa-miR-323a-3p	26	hsa-miR-146a-5p
2	hsa-miR-378f	27	hsa-miR-3158-5p	2	hsa-miR-335-3p	27	hsa-miR-125b-1-3p
3	hsa-miR-3909	28	hsa-miR-4637	3	hsa-miR-328-3p	28	hsa-miR-27a-3p
4	hsa-miR-4477a	29	hsa-miR-185-5p	4	hsa-miR-204-3p	29	hsa-miR-145-5p
5	hsa-miR-4520-5p	30	hsa-miR-4670-5p	5	hsa-miR-654-5p	30	hsa-miR-382-5p
6	hsa-miR-362-5p	31	hsa-miR-4758-5p	6	hsa-miR-16-5p	31	hsa-miR-127-3p
7	hsa-miR-718	32	hsa-miR-3144-3p	7	hsa-miR-210-3p	32	hsa-miR-148a-3p
8	hsa-miR-548am-3p	33	hsa-miR-4704-5p	8	hsa-miR-27a-5p	33	hsa-miR-769-5p
9	hsa-miR-4760-5p	34	hsa-miR-3199	9	hsa-miR-28-3p	34	hsa-miR-409-3p
10	hsa-miR-590-3p	35	hsa-miR-2909	10	hsa-miR-92b-3p	35	hsa-miR-151a-5p
11	hsa-miR-3186-3p	36	hsa-miR-633	11	hsa-miR-378a-3p	36	hsa-miR-671-3p
12	hsa-miR-15a-5p	37	hsa-miR-3163	12	hsa-miR-320c	37	hsa-let-7c-5p
13	hsa-miR-513b-5p	38	hsa-miR-545-3p	13	hsa-miR-486-5p	38	hsa-miR-432-5p
14	hsa-miR-4797-3p	39	hsa-miR-192-5p	14	hsa-miR-23b-3p	39	hsa-miR-151a-3p
15	hsa-miR-619-3p	40	hsa-miR-4755-3p	15	hsa-let-7d-3p	40	hsa-miR-221-3p
16	hsa-miR-4310	41	hsa-miR-432-5p	16	hsa-miR-134-5p	41	hsa-miR-25-3p
17	hsa-miR-4725-3p	42	hsa-miR-3136-5p	17	hsa-miR-34a-5p	42	hsa-miR-543
18	hsa-miR-4797-5p	43	hsa-miR-548e-3p	18	hsa-miR-423-5p	43	hsa-miR-100-5p
19	hsa-miR-4638-3p	44	hsa-miR-3189-3p	19	hsa-miR-22-3p	44	hsa-miR-192-5p
20	hsa-miR-339-3p	45	hsa-miR-1973	20	hsa-miR-146b-5p	45	hsa-let-7e-5p
21	hsa-miR-4736	46	hsa-miR-335-5p	21	hsa-miR-30a-3p	46	hsa-miR-532-5p
22	hsa-miR-1270	47	hsa-miR-3617-5p	22	hsa-miR-320a	47	hsa-miR-937-3p
23	hsa-miR-766-3p	48	hsa-miR-154-5p	23	hsa-miR-483-5p	48	hsa-let-7i-5p
24	hsa-miR-4275	49	hsa-miR-1288-3p	24	hsa-miR-99b-5p	49	hsa-miR-941
25	hsa-miR-3125	50	hsa-miR-544a	25	hsa-miR-370-3p	50	hsa-miR-99a-5p

Supplementary Table S2. Target genes of miR-192-5p and miR-432-5p validated with at least three assays.

miRNA	Target	Number of assays to validate target
hsa-miR-192-5p	ALCAM	5
	CDC7	5
	CUL5	5
	ERCC3	5
	LMNB2	5
	MAD2L1	5
	PIM1	5
	ERCC4	4
	RB1	4
	BCL2	4
	DLG5	4
	DTL	4
	HRH1	4
	MCM10	4
	MIS12	4
	KIF20B	4
	PRPF38A	4
	RACGAP1	4
	SEPT10	4
	SMARCB1	4
	WNK1	4
	XIAP	4
	DICER1	4
	ACVR2B	3
	CAV1	3
	SCN5A	3
hsa-miR-432-5p	MECP2	3
	RCOR1	3
	NES	3

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