Supplementary materials

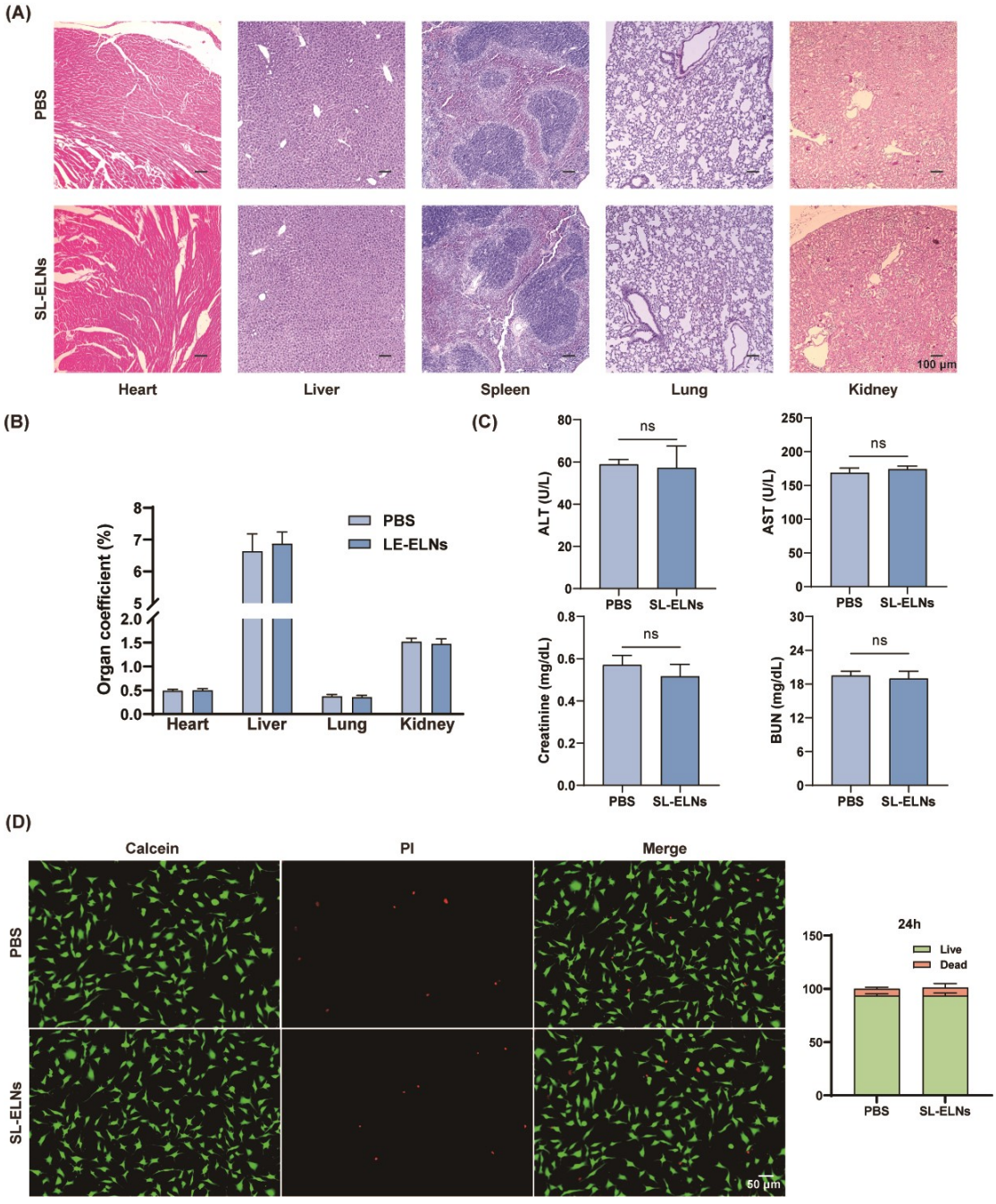

Figure S1. Biocompatibility assay of SL-ELNs.
(A) Hematoxylin and eosin (HE) staining(n=3). (B) Organs coefficients(n=3). (C) Liver function-related parameter (serum ALT and AST) and kidney function-related parameters (BUN and serum creatinine) (n=6). (D) Calcein AM/PI staining(n=3). Data are expressed as mean ± SD (ns, not significant, *P<0.05, **P<0.01, and ***P<0.005 were determined by a student's t-test).

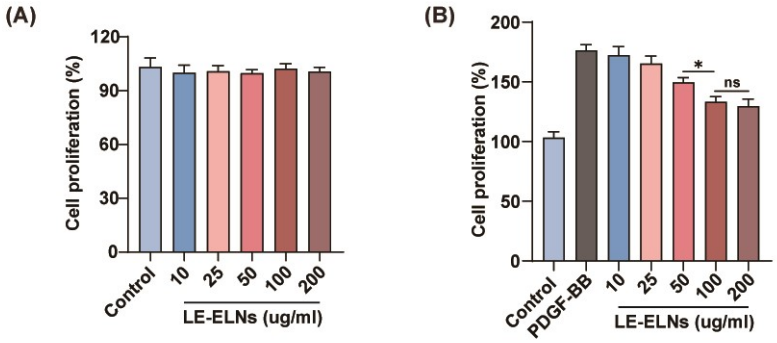

Figure S2. The effect of SL-ELNs on VSMCs treated with (A) or without (B) PDGF-BB analyzed by CCK-8.

Data are expressed as mean±SD (**P*<0.05, ***P*<0.01 and ****P*<0.005 were determined by one-way ANOVA and Tukey's post hoc test)

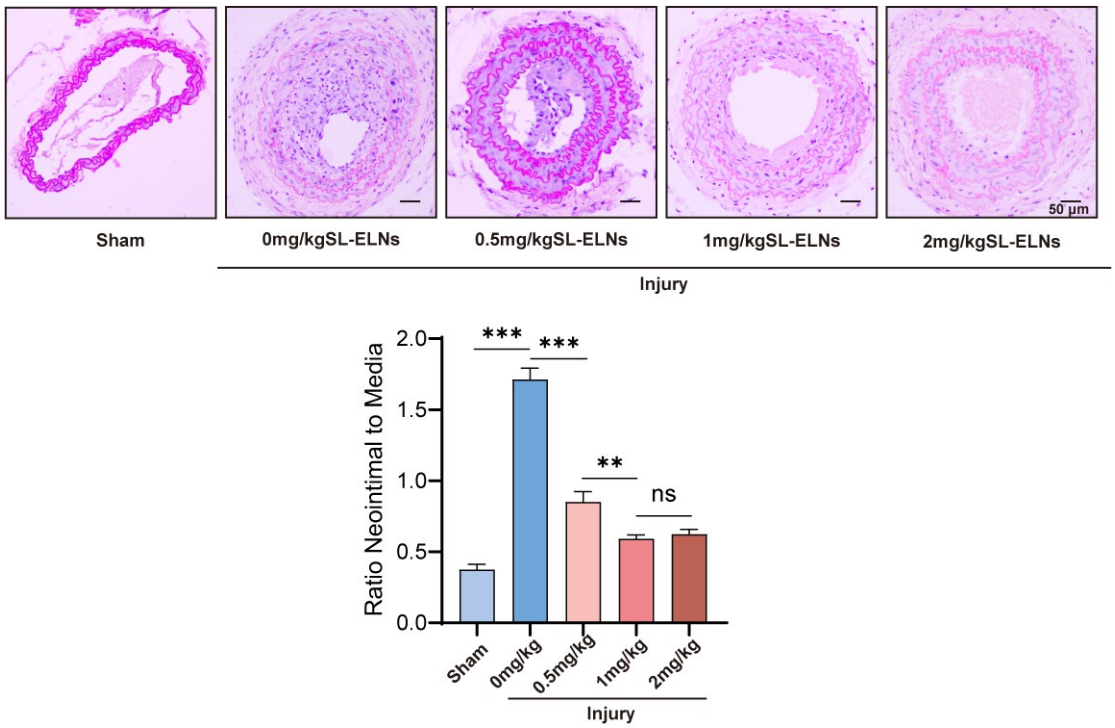

Figure S3 HE staining of mouse carotid artery vascular (n=3).

Data are expressed as mean±SD (**P*<0.05, ***P*<0.01 and ****P*<0.005 were determined by one-way ANOVA and Tukey's post hoc test)

Figure S4. LE-ELNs improves oxidative stress induced by PDGF-BB PDGF-BB (A) ROS levels evaluated using the DCFH-DA staining assay. (B) Mitochondrial membrane potential evaluated using the JC-1 assay.

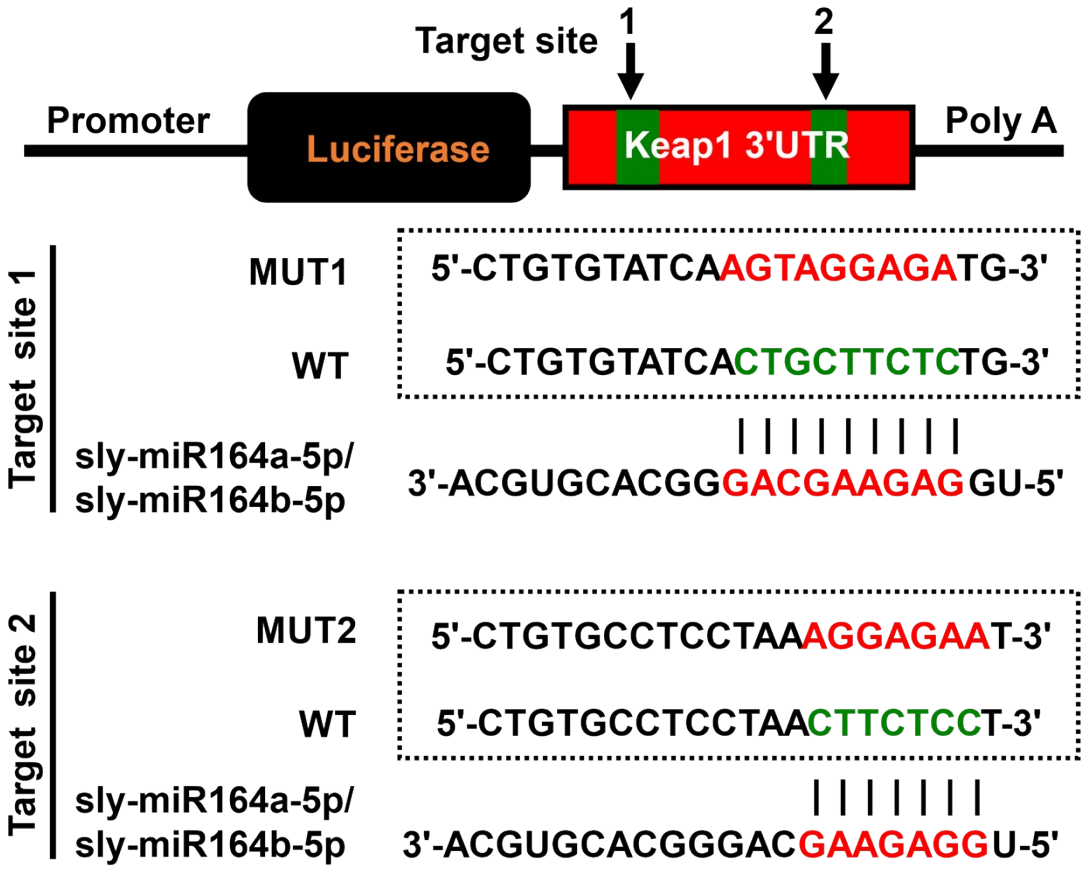

Figure S5. Potential binding sites between miRNA-164a/b-5p and the 3'UTR of Keap1

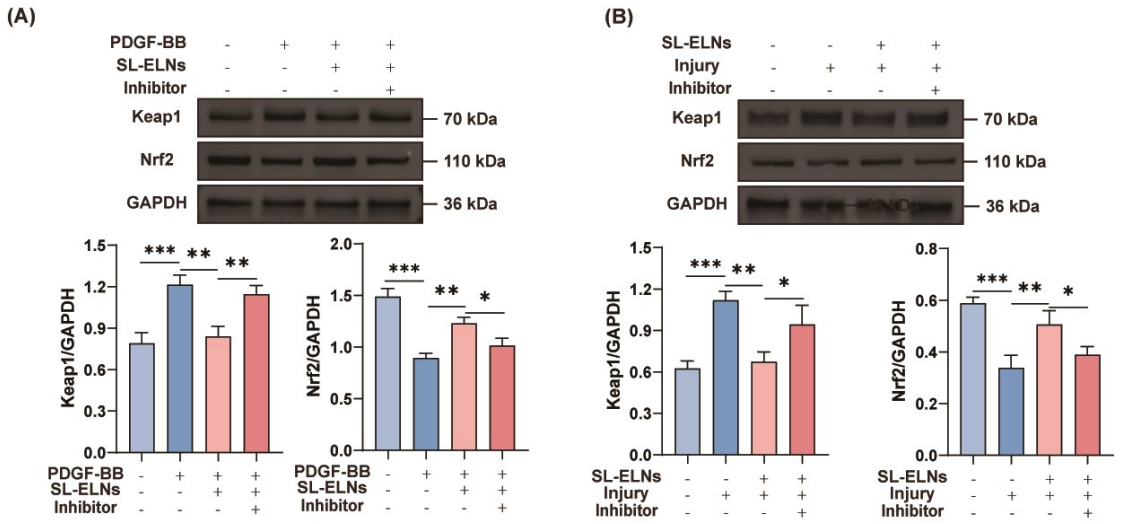

Figure S6. Potential binding sites between miRNA-164a/b-5p and the 3'UTR of Keap1

Western blot and quantitative analysis of Keap1 and Nrf2 in VSMCs (A) and vascular (B) (n = 4). Data are expressed as mean±SD (**P*<0.05, ***P*<0.01 and ****P*<0.005 were determined by one-way ANOVA and Tukey's post hoc test)

Table S1 The size diameter, Zeta potential and concentration of TNVs from three different layers.

Samples	Size diameter (nm)	Zeta potential (mV)	Concentration (Particles / mL)
TNVs 8-30%	146.9±57.3	23.3±2.1	1.7E+7
TNVs 30-45%	127.3±50	28.3±3.5	2.2E+10
TNVs 45-60%	127.4±61.3	22.7±3.1	1.5E+6

Table S2 Known miRNA expression

miRNAname	Length	Total Count
sly-miR10528	21	178
sly-miR10529	24	6
sly-miR10530	24	2
sly-miR10531	23	6
sly-miR10532	24	622
sly-miR10533	22	3
sly-miR10534	21	347
sly-miR10535a	24	3
sly-miR10535b	24	19

sly-miR10537	21	83
sly-miR10538	24	117
sly-miR10542	23	24
sly-miR156a	21	28
sly-miR156b	21	28
sly-miR156c	21	28
sly-miR156d-3p	22	2
sly-miR156d-5p	20	31
sly-miR156e-3p	21	5
sly-miR156e-5p	20	15
sly-miR159	21	2008
sly-miR159b	21	1
sly-miR160a	21	145
sly-miR162	21	410
sly-miR164a-3p	21	92
sly-miR164a-5p	21	9355
sly-miR164b-5p	21	9274
sly-miR166a	21	2477
sly-miR166b	21	2383
sly-miR166c-3p	21	723
sly-miR166c-5p	21	82
sly-miR167a	21	10
sly-miR167b-3p	21	77
sly-miR167b-5p	22	51
sly-miR168a-3p	21	101
sly-miR168a-5p	21	750
sly-miR168b-3p	21	539
sly-miR168b-5p	21	750
sly-miR169a	21	6
sly-miR169b	21	2
sly-miR169c	21	4
sly-miR169d	21	6
sly-miR169e-3p	21	2
sly-miR169e-5p	22	2
sly-miR169f	21	2
sly-miR171a	21	27
sly-miR171b-3p	21	9
sly-miR171e	21	54
sly-miR171f	21	5
sly-miR172a	21	44
sly-miR172b	21	44
sly-miR172c	21	30
sly-miR172d	21	34
sly-miR1916	20	3

sly-miR1917	21	2
sly-miR1918	22	1
sly-miR1919a	21	1390
sly-miR1919b	21	1390
sly-miR1919c-3p	21	1390
sly-miR1919c-5p	21	627
sly-miR319a	20	4
sly-miR319b	21	3
sly-miR319c-3p	21	4
sly-miR390a-3p	21	54
sly-miR390a-5p	21	26
sly-miR390b-3p	21	112
sly-miR390b-5p	21	137
sly-miR391	22	4
sly-miR394-5p	20	10
sly-miR395a	22	9
sly-miR395b	22	9
sly-miR396a-3p	21	611
sly-miR396a-5p	21	928
sly-miR396b	21	652
sly-miR397-3p	21	4
sly-miR398a	21	76
sly-miR399	21	495
sly-miR399b	21	19
sly-miR403-3p	21	746
sly-miR403-5p	21	12
sly-miR477-3p	22	3
sly-miR477-5p	21	23
sly-miR482a	22	202
sly-miR482b	22	1424
sly-miR482c	22	161
sly-miR482d-3p	22	128
sly-miR482d-5p	21	67
sly-miR482e-3p	22	365
sly-miR482e-5p	21	24
sly-miR530	21	1
sly-miR5300	22	6
sly-miR5302b-5p	22	1
sly-miR5303	21	1
sly-miR5304	21	3
sly-miR6022	21	1163
sly-miR6023	22	11
sly-miR6024	22	324
sly-miR6025	22	2

sly-miR6026	22	1247
sly-miR6027-3p	22	306
sly-miR6027-5p	22	140
sly-miR7981a	24	72
sly-miR7981b	24	191
sly-miR7981c	24	83
sly-miR7981d	24	82
sly-miR7981e	24	326
sly-miR7981f	24	198
sly-miR827	21	1
sly-miR9470-3p	20	1241
sly-miR9470-5p	21	163
sly-miR9471a-3p	21	932
sly-miR9471a-5p	21	23
sly-miR9471b-3p	21	3264
sly-miR9471b-5p	21	6
sly-miR9472-5p	21	4
sly-miR9473-3p	21	1
sly-miR9473-5p	21	4
sly-miR9474-5p	22	2
sly-miR9475-3p	21	13
sly-miR9475-5p	21	8
sly-miR9476-3p	21	219
sly-miR9476-5p	21	27
sly-miR9478-3p	21	2
sly-miR9479-3p	22	19
sly-miR9479-5p	22	3

Table S3 novel miRNA expression

miRNA name	Sequence	Length	Total Count
novel-miRNA-10-5p	TGTGTCTGTGTGGGTGTGGGGT	20	18
novel-miRNA-11-5p	TGTGTCTGTGTGGGTGTGGGGT	20	18
novel-miRNA-12-3p	TGCCAAAGGAGAATTGCCCTG	21	82
novel-miRNA-12-5p	GTGCAATTCTCCTTTGGCAAA	21	1
novel-miRNA-13-3p	TCGATAAACCTCTGCATCCAG	21	2
novel-miRNA-13-5p	GGAGGCAGCGGTTCATCGATC	21	31
novel-miRNA-14-3p	AAGATAGTGTCACCTAGGCCG	21	58
novel-miRNA-15-5p	GGAGGATTAAGTTTGAGATA	22	10
novel-miRNA-1-5p	AGGTAGTTGCTTGTCACCTCA	21	20
novel-miRNA-16-5p	GAGAGAAGAGTGCATAGTTG	20	140
novel-miRNA-17-3p	AGTGGCTTGTACATGTGACA	21	15
novel-miRNA-18-5p	AACCAAGGTAAAGAGTTCTA	20	42
novel-miRNA-19-3p	TCGATAAACCTCTGCATCCAG	21	2

novel-miRNA-19-5p	GGAGGCAGCGGTTCATCGATC	21	31
novel-miRNA-20-5p	GAGACTTGTGCATGTGACAA	21	14
novel-miRNA-21-3p	AGCTAGTGCCACGTAGGTCA	20	294
novel-miRNA-21-5p	GCCTACGTGACATTGTCTTG	20	6
novel-miRNA-22-5p	GACTAGTTTTGGGTTGTGCT	20	245
novel-miRNA-23-3p	AAGATAGTGCCACATAGACCA	21	103
novel-miRNA-23-5p	GCCTACGTGGAACTAGCTTGA	21	14
novel-miRNA-24-5p	GATAACTTCGGATGACCGTCA	20	14
novel-miRNA-25-3p	GGCAACGGATTTGTATTGACGT	22	15
novel-miRNA-2-5p	AGGTGACGATTGGAACATGTC A	22	66
novel-miRNA-26-5p	GATTCTGGTGGCTATGGGGGC	21	39
novel-miRNA-27-3p	GAGGTAAGATAGTAAGGACC	20	21
novel-miRNA-27-5p	CCCTTATTATCTTATCTCTT	20	22
novel-miRNA-28-3p	GTTCCCTTGACCGCTTCATT	22	18
novel-miRNA-29-3p	AGTTAGAGGGCATAGATGTCA	21	12
novel-miRNA-30-5p	GATCTTCTGATGTCTTAGCCC	21	13
novel-miRNA-31-3p	GCTTGGTAGTACTTATTGTCAA	20	10
novel-miRNA-32-3p	AAGATAGTGTCACGTAGGTCA	21	104
novel-miRNA-33-5p	GCAAGGTAAGATCGAATGGTA C	22	48
novel-miRNA-34-5p	GCAGCATCATCAAGATTCACA	21	43
novel-miRNA-35-5p	TGTAACGACCTGTTTAGTCA	20	269
novel-miRNA-3-5p	GTCACATGTCTTCATTTGATT	20	15
novel-miRNA-36-5p	GACTAGTTTTGGGTTGTGCT	20	245
novel-miRNA-37-5p	GCAGCATCATCAAGATTCACA	21	44
novel-miRNA-38-3p	CTAGGAGATATATGGAGACCC A	20	15
novel-miRNA-39-3p	GTTCCCTTGACCGCTTCATT	22	18
novel-miRNA-40-3p	AGATAGACTTGTTTAAATCTCA	22	19
novel-miRNA-41-3p	GATGATGAAGTTGGATGAGGC	21	535
novel-miRNA-42-3p	GTTTGTGATGTTCAGCTTATCG	22	16
novel-miRNA-4-5p	GTGCGAGGGGGCGACGCGAT	20	1836
novel-miRNA-5-3p	AAGATAGTGTCACGTAGGCCG	21	202
novel-miRNA-5-5p	GCCTAAGTGACACTATTTTGT	21	12
novel-miRNA-6-3p	TATTTCTGCAGCTTTGGAATT	21	31
novel-miRNA-7-3p	CGATTTTGCCCTTTTGGTCA	20	19
novel-miRNA-8-5p	GCAAGGTAAGATCGAATGGTA C	22	48
novel-miRNA-9-5p	AGTGGCTTGTACATGTGACA	22	15

Table S4 The sequences of qPCR primers.

miRNA	Reverse primer sequence (5’-3’)
miRNA164a/b-5p	GTCGTATCCAGTGCAGGGTCCGAGGTATTC

	GCACTGGATACGACTGCACG
miRNA9471b-3p	GTCGTATCCAGTGCAGGGTCCGAGGTATTC GCACTGGATACGACCAGTGA
miRNA166a/b	GTCGTATCCAGTGCAGGGTCCGAGGTATTC GCACTGGATACGACGGGGAA
miRNA159	GTCGTATCCAGTGCAGGGTCCGAGGTATTC GCACTGGATACGACTAGAGC
novel-miRNA-4-5p	GTCGTATCCAGTGCAGGGTCCGAGGTATTC GCACTGGATACGACTCGCGT