Supplementary Files

Figure S1. Immunophenotypic analysis of the surface markers CD34 and CD45 in MSCs.

Figure S2. Oil Red O staining of different passage MSCs (P5 and P18) at 2 weeks. .

Figure S3. Alizarinl Red S staining of different passage MSCs (P5, 18) at 2 weeks.

Figure S4. Network of DEMs targets to DEGs.

Figure S5. The expression of the key miRNAs in MSCs and MSC-MVs during senescence.

**Figure S6**. The expression of the key miRNAs in MSCs and MSC-MVs under reduced serum culture conditions.

Table S1. MSCs and MSC-MVs miRNA reads filtering and mapping statistics.

Table S2. MSCs and MSC-MVs mRNA reads filtering and mapping statistics.

 Table S3. The specific primer sequences.



Figure S1. Immunophenotypic analysis of the surface markers CD34 and CD45

in MSCs. MSCs were negetive for CD34 and CD45 at P4, 14 and 22.



**Figure S2. Oil Red O staining of different passage MSCs (P5 and P18) at 2 weeks**. Percentage of oil red O positive area over total area was analyzed using Image J software. n =3. Abbreviations: CM: complete medium; AIM: adipogenic induction medium.



Figure S3. Alizarinl Red S staining of different passage MSCs (P5, 18) at 2 weeks.

Percentage of alizarin red-positive area over total area was analyzed using Image J software. n = 3. Abbreviations: CM: complete medium; OIM: osteogenic induction medium.



Figure S4. Network of DEMs targets to DEGs.



**Figure S5. Expression of the key miRNAs in MSCs and MSC-MVs during senescence.** Expression of miR-148a-3p, miR-204-5p, miR-301a-3p, miR-301b and miR-335-5p in MSCs and MSC-MVs analyzed by RT-PCR.



Figure S6. Expression of the key miRNAs in MSCs and MSC-MVs under reduced serum culture conditions. Expression of miR-148a-3p, miR-204-5p, miR-301a-3p, miR-301b and miR-335-5p in MSCs and MSC-MVs analyzed by RT-PCR.

Sample	Filtered	Mapped	<b>Filtered-Per</b>	Mapped-Per
	reads	reads		
EP MSCs	14893002	14452685	79.99%	97.04%
LP MSCs	12661391	12254480	74.61%	96.79%
EP MSC-MVs	6938623	6692487	34.39%	96.45%
LP MSC-MVs	4460356	4318609	26.04%	96.82%

Table S1. MSCs and MSC-MVs miRNA reads filtering and mapping statistics.

Abbreviations: EP: early passage; LP: Late passage.

Table S2. MSCs and MSC-MVs mRNA reads filtering and mapping statistics.

Sample Raw		Filtered Mapped		<b>Filtered-Per</b>	Mapped-Per
	reads	reads	reads		
EP MSCs	65684320	63311018	50385791	96.39%	79.58%
LP MSCs	67331890	64949474	52452641	96.46%	80.76%
EP MSC-MVs	74271816	53022882	33543006	71.39%	63.26%
LP MSC-MVs	77209858	56430144	30107364	73.09%	53.35%

Abbreviations: EP: early passage; LP: Late passage.

Gene	Forward (5' to 3')	Reverse (5' to 3')
β-actin	CACGATGGAGGGGCCGGACTCA	TAAAGACCTCTATGCCAACACAG
	TC	Т
p16	ACCAGAGGCAGTAACCATGC	AAGTTTCCCGAGGTTTCTCA
p21	CTGGAGACTCTCAGGGTCGAA	CGGATTAGGGCTTCCTCTTG
ALP	AACACCACCCAGGGGAAC	TGGCATGGTTCACTCTCGT
RUNX2	AATGGTTAATCTCCGCAGGTC	TTCAGATAGAACTTGTACCCTCTG
		TT
OCN	AGCAAAGGTGCAGCCTTTGT	GCGCCTGGGTCTCTTCACT
DCN	ACCAGCATTCCTCAAGGTCTTC	CTCCCTCAGATGAGGCGTGT
HNRNPD	GAGGCCTTAGCTGGGACACTAC	CAGGTGTATCTGGAGAAAGGCC
CD276	GCTCAACCTCATCTGGCAGC	CATGCTGGGCTTCGAGTAGG
PDGFRA	GAAGTGAAAGGCAAAGGCATC	AGCTTCCAACTGGCTGAAGG
BHLHE41	CCTTAACCGAGCAACAGCATC	GCATGTTTGAAATCCCGAGTG
IGFBP5	ACCCAGTCCAAGTTTGTCGG	TCATCCCGTACTTGTCCACG
NFIX	TCTACAAGTCGCCTCAGTGCTC	CCTGGAAACTTAAGTGCCCG

Table	<b>S3</b> .	The	specific	primer	sequences.
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