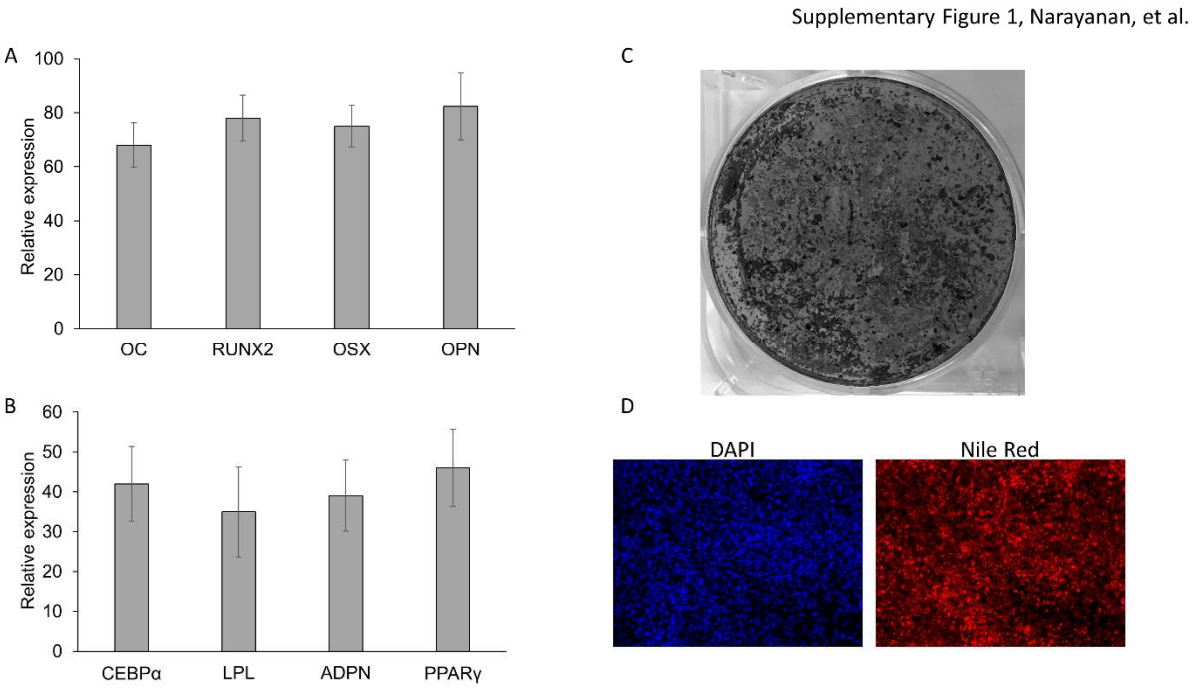
Supplementary Table 1

List of primers

Osteogenic primers	**Assay #**
RUNX2	Hs01047973_m1
Osterix	Hs01866874_s1
OC	Hs01587814_g1
OPN	Hs00959010_m1
Adipogenic primers	**Assay #**
C/EBPa	Hs00269972_s1
LPL	Hs00173425_m1
PPARg	Hs01115513_m1
ADPN	Hs00605917_m1
miRNA	**Assay #**
hsa-miR-34a	478048_mir
hsa-miR-27a	477998_mir
hsa-miR-22	477985_mir
hsa-miR-143	478713_mir
hsa-miR-375	478074_mir
hsa-miR-10a	479241_mir
U6 snRNA	1973

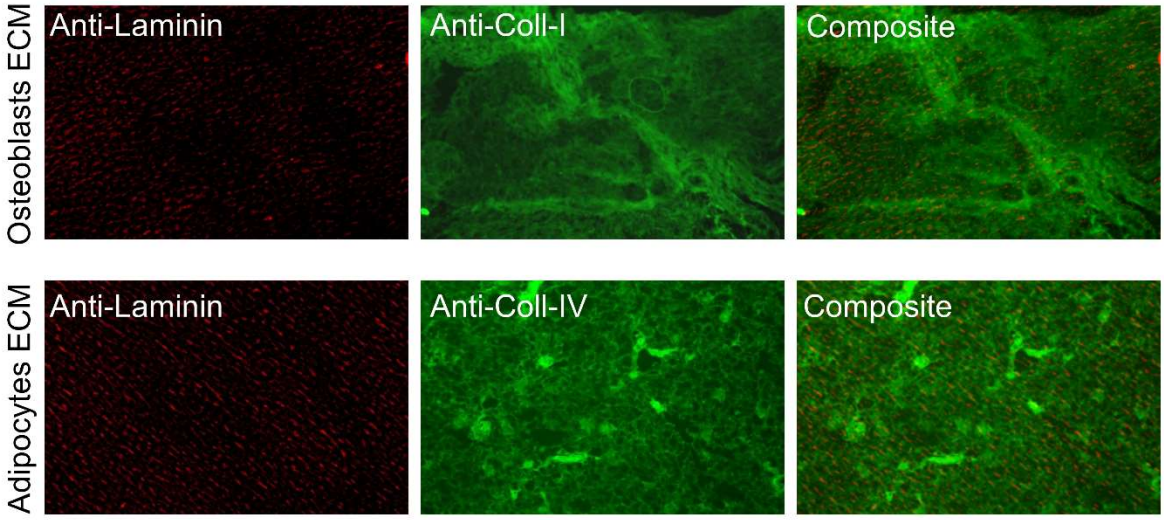
List of antibodies

Antibody	**Company**
CD9 Antibody (C-4): sc-13118	Santa Cruz
CD63 Antibody (H-193): sc-15363	Santa Cruz
TSG 101 Antibody (C-2): sc-7964	Santa Cruz
Tubulin Antibody (B-7): sc-5286	Santa Cruz
Actin Antibody (C4): sc-47778	Santa Cruz
Anti-Hsp90 antibody (ab13495)	Abcam
Anti-RUNX2 antibody (ab23981)	Abcam
OSX Antibody (F-3): sc-393325	Santa Cruz
PPAR gamma Antibody (PA3-821A)	ThermoFisher Scientific
C/EBP alpha Antibody (D-5): sc-365318	Santa Cruz



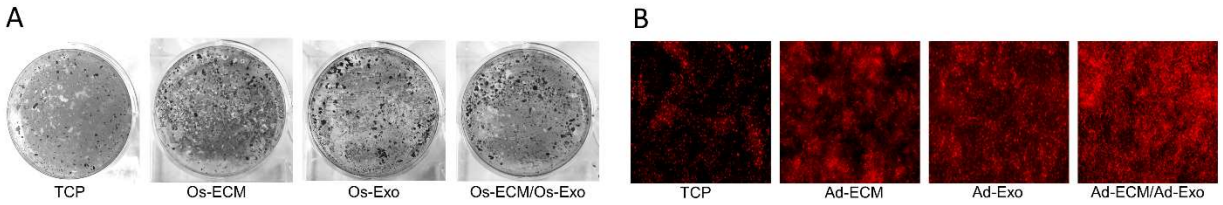
Supplementary Figure 1:

Normal human osteoblasts (NHO) and pre-adipocytes were differentiated either into osteoblasts or adipocytes with respective differentiation medium. Relative fold expression of osteogenic (A) and adiogenic (B) genes were calculated with undifferentiated hMSCs as 1 fold expression. Upon differentiation into osteoblasts, the deposition of calcium phosphate was confirmed by vonKossa staining (C). Presence of lipid droplets were detected by Nile Red staining together with nuclear staining by DAPI (D)



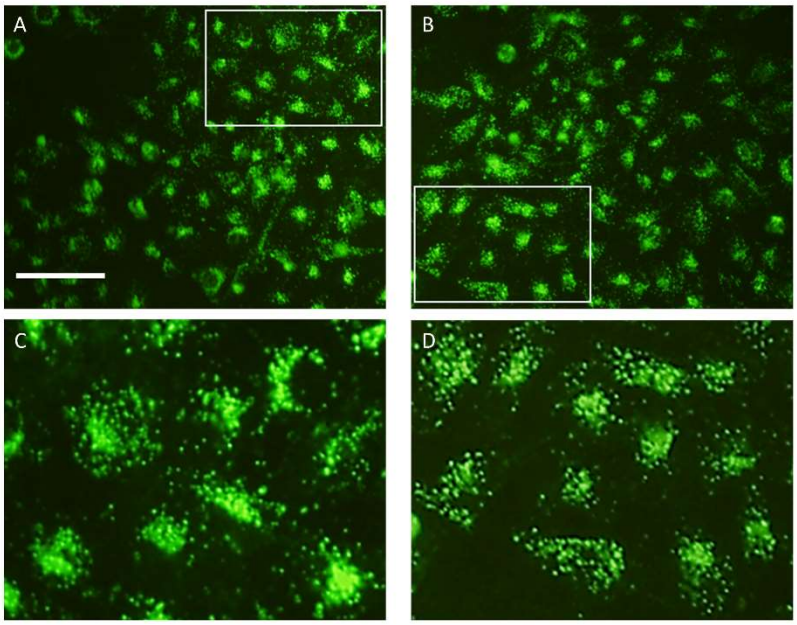
Supplementary Figure 2:

The cell-secreted ECM from partially differentiated osteoblasts and adipocytes were immunostained with antibodies against laminin, collagens type-I and type-IV.



Supplementary Figure 3:

The human mesenchymal stem cells (hMSCs) were differentiated on either tissue culture plate (TCP) or extracellular matrix (ECM). During osteogenic differentiation on osteoblast ECM (Os-ECM), the cells were also supplemented and differentiated in the presence of osteoblast exosomes (Os-ECM/Os-Exo). The calcium deposition was visualized using von Kossa staining (A). During adipogenic differentiation on adipocyte ECM (Ad-ECM), the cells were also supplemented and differentiated in the presence of adipocyte exosomes (Ad-ECM/Ad-Exo). Lipid droplets were visualized using Nile Red (B).



Supplementary Figure 4:

Exosome uptake in human mesenchymal stem cells. Adhered human mesenchymal stem cells (hMSCs) were incubated with either labeled osteoblast exosomes for 24 h, as described in Materials and Methods section. Exosomes were isolated from either differentiated osteoblasts (A) or differentiated adipocytes (B). Following incubation, the cells were washed with PBS, fixed with paraformaldehyde and visualized under fluorescent microscope. Figure (C) and (D) represent labeled exosomes visualized under higher magnification of the boxed area from (A) and (B), respectively. Scale bar = 200 μm.

Figure 5A

	OC	RUNX2	OSX	OPN
TCP	175 ± 56	150 ± 43	110 ± 53	95 ± 35
Os-ECM	355 ± 65	255 ± 55	215 ± 45	221 ± 28
Os-Exo	450 ± 82	280 ± 81	220 ± 72	380 ± 81
Os-ECM+Os-Exo	750 ± 90	550 ± 100	450 ± 80	650 ± 93

Figure 5B

	C/EBPα	LPL	ADPN	PPARγ
TCP	95 ± 35	76 ± 32	72 ± 25	60 ± 15
Ad-ECM	290 ± 25	272 ± 28	170 ± 21	265 ± 22
Ad-Exo	430 ± 93	300 ± 62	350 ± 58	370 ± 62
Ad-ECM+Ad-Exo	650 ± 109	450 ± 108	460 ± 99	650 ± 104

Figure 8A and 8B

	OC	RUNX2	OSX	C/EBPα	ADPN	PPARγ
Os-ECM	4 ± 1.5	3 ± 0.84	2.5 ± 0.87	0.15 ± 0.15	0.1 ± 0.16	0.17 ± 0.09
Os-ECM + Os-Exo	17 ± 4	7 ± 1.5	10 ± 2.7	0.12 ± 0.12	0.14 ± 0.1	0.15 ± 0.09
Os-ECM + Ad-Exo	5 ± 3.5	2.5 ± 0.98	2.12 ± 0.84	2.9 ± 0.5	2.1 ± 0.6	1.8 ± 0.6

Figure 8C and 8D

Ad-ECM	0.18 ± 0.09	0.13 ± 0.09	0.12 ± 0.08	6 ± 1.5	5 ± 0.64	3.8 ± 0.67
Ad-ECM + Ad-Exo	0.17 ± 0.11	0.12 ± 0.09	0.13 ± 0.07	9.5 ± 1.85	7.4 ± 1.91	7.8 ± 1.61
Ad-ECM + Os-Exo	1.5 ± 0.65	2.2 ± 0.78	2.1 ± 0.45	2.9 ± 0.86	4 ± 1.1	3.5 ± 0.87

Supplementary Table 2:

Values associated to the fold changes of gene expression presented in Figure 5 and 8 are given in the table