

ORIGINAL RESEARCH ARTICLE

Bone organoid-derived extracellular vesicles promote angiogenesis and osteogenesis *in vitro*

Supplementary File

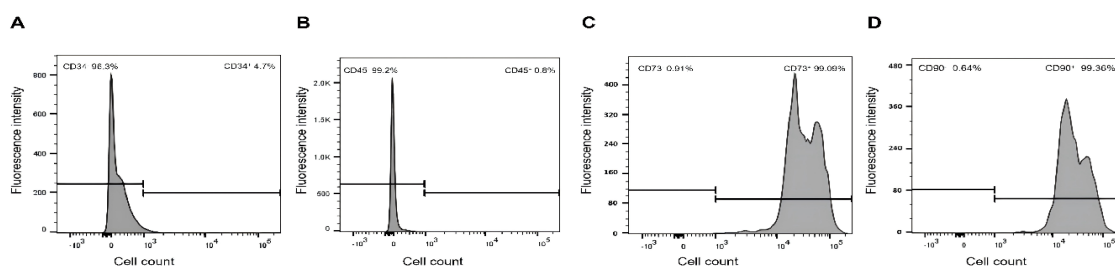


Figure S1. Flow cytometry analysis of bone marrow mesenchymal stem cell surface biomarkers. (A) CD34. (B) CD45. (C) CD73. (D) CD90.

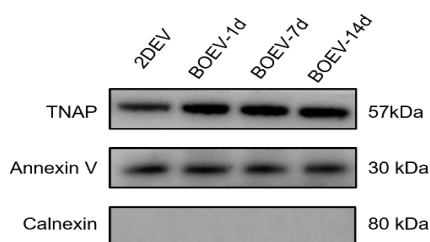


Figure S2. Western blot detection of matrix vesicle-related markers and calnexin (a negative marker of EVs) ($n = 3$)
Abbreviation: TNAP: Tissue-nonspecific alkaline phosphatase.

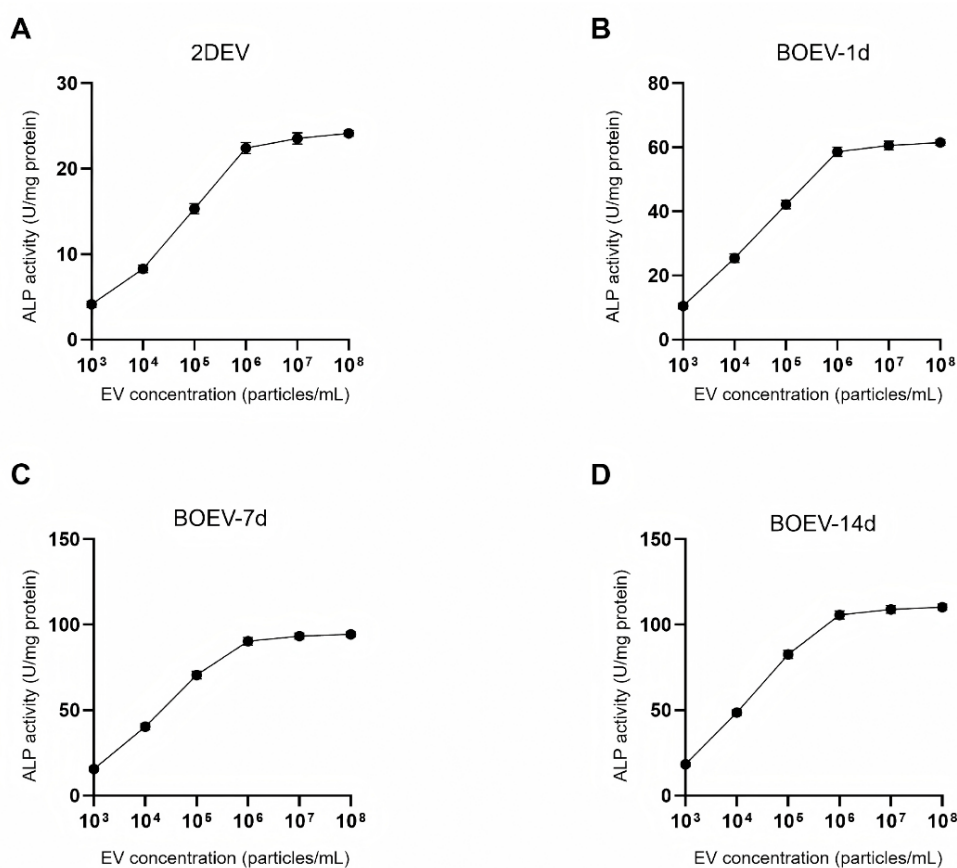


Figure S3. Dose–response relationship and determination of the standardized working concentration for bone organoid-derived extracellular vesicles (BOEVs). (A–D) Sigmoidal dose-response curves illustrating functional activity across a concentration gradient (10^3 to 10^8 particles/mL) for 2DEV (A), BOEV-1d (B), BOEV-7d (C), and BOEV-14d (D) ($n = 3$). Abbreviations: ALP: Alkaline phosphatase; EV: Extracellular vesicle.

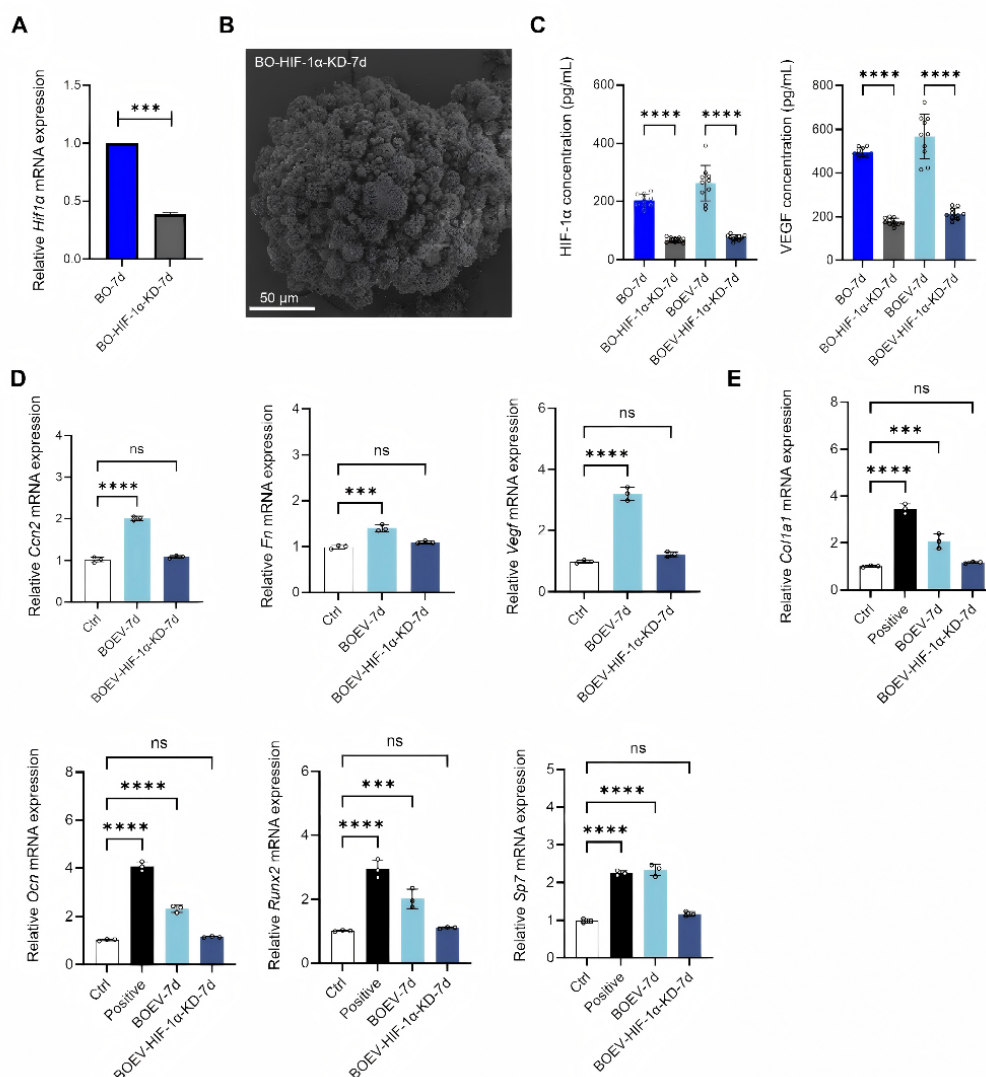


Figure S4. Effects of *Hif1a* knockdown on angiogenic factors in bone organoid-derived extracellular vesicles (BOEVs). (A) Real-time quantitative polymerase chain reaction (RT-qPCR) analysis of *Hif1a* messenger RNA (mRNA) expression in bone organoids (BOs). (B) Scanning electron microscopy (SEM) images of BO-HIF-1α-KD-7d. Scale bar: 50 μm; magnification: 800×. (C) Enzyme-linked immunosorbent assay (ELISA) quantification of hypoxia-inducible factor-1α (HIF-1α) and vascular endothelial growth factor (VEGF) concentrations in extracellular vesicles (EVs) ($n = 10$). (D) RT-qPCR analysis of relative mRNA expression of angiogenesis-related genes (*Ccn2*, *Fn*, and *Vegf*) in human umbilical vein endothelial cells (HUVECs) ($n = 3$). (E) RT-qPCR analysis of relative mRNA expression of osteogenesis-related genes (*Col1a1*, *Ocn*, *Runx2*, and *Sp7*) in hFOB1.19 cells ($n = 3$). Notes: *** $p < 0.001$, **** $p < 0.0001$, ns: $p > 0.05$.

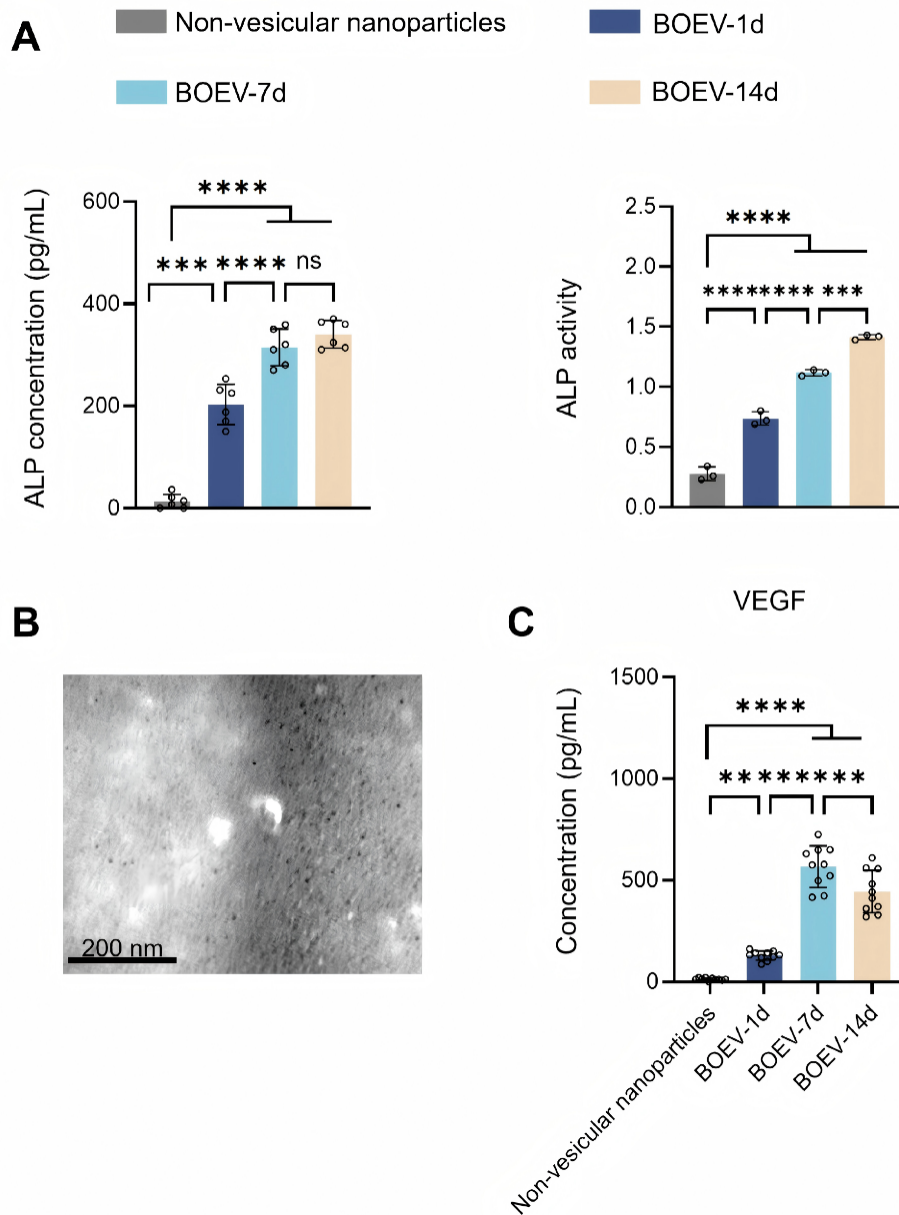


Figure S5. The effect of non-vesicular nanoparticles on osteogenesis and angiogenesis. (A) Detection of alkaline phosphatase (ALP) concentration ($n = 6$) and ALP activity ($n = 3$). (B) Transmission electron microscopy observation of non-vesicular nanoparticles morphology. Scale bar: 200 nm; magnification: 30,000 $\times$. (C) Detection of vascular endothelial growth factor (VEGF) concentration ($n = 10$). Notes: $**p < 0.01$, $***p < 0.001$, $****p < 0.0001$, ns: $p > 0.05$.

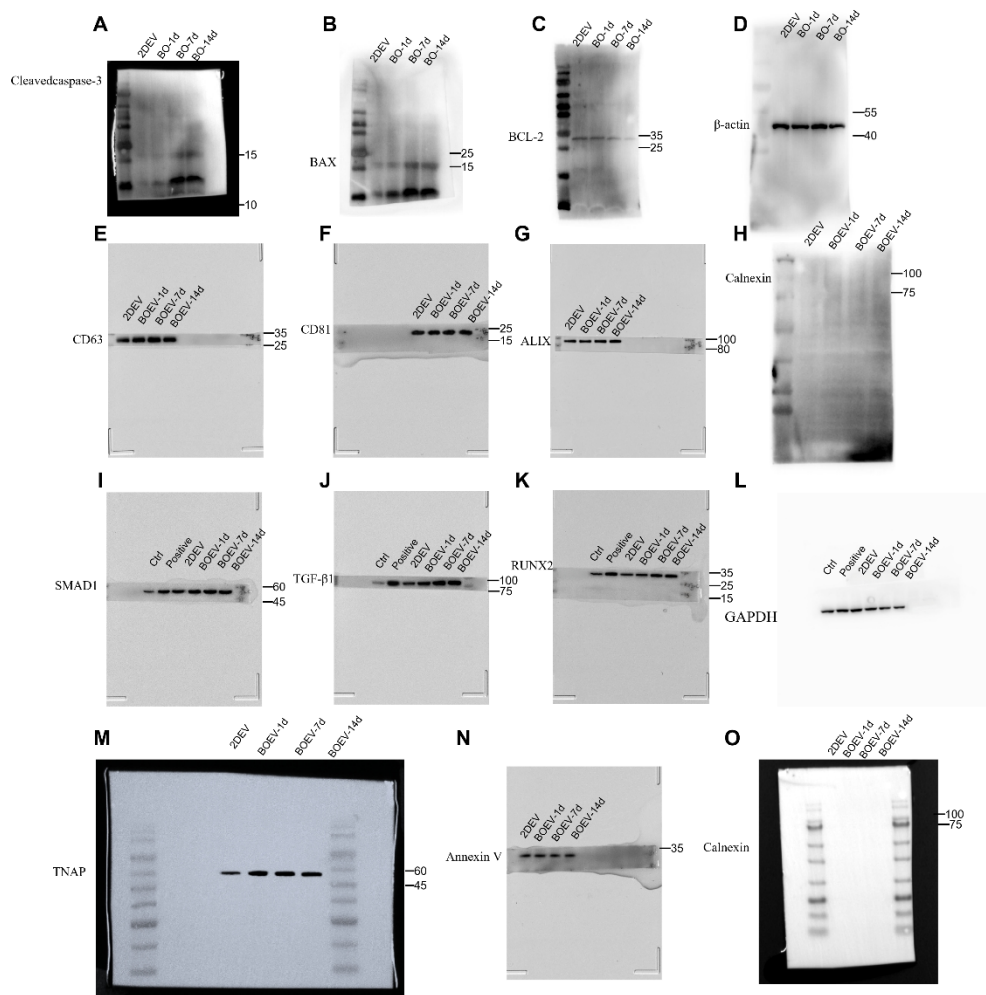


Figure S6. Uncropped original Western blot images. (A–D) Uncropped original blots of apoptosis-related proteins in bone organoids, including cleaved caspase-3 (A), BAX (B), BCL-2 (C), and β-actin (D), corresponding to Figure 11. (E–H) Uncropped original blots of extracellular vesicle markers, including CD63 (E), CD81 (F), ALIX (G), and the negative marker calnexin (H), corresponding to Figure 3E. (I–L) Uncropped original blots of osteogenic-related molecules in hFOB1.19 cells, including SMAD1 (I), TGF-β1 (J), RUNX2 (K), and GAPDH (L), corresponding to Figure 7D. (M–O) Uncropped original blots of matrix vesicle-related markers, including TNAP (M), annexin V (N), and the negative marker calnexin (O), corresponding to Figure S2.

Table S1. The detailed list of 270 differentially expressed genes

Gene	2D-cultured BMSCs_1	2D-cultured BMSCs_2	2D-cultured BMSCs_3	BO-1d_1	BO-1d_2	BO-1d_3	BO-7d_1	BO-7d_2	BO-7d_3	BO-14d_1	BO-14d_2	BO-14d_3
Clic1	0.625	0.926	0.422	-0.479	-0.170	-0.717	1.357	1.153	1.162	0.410	0.146	0.133
Ptprf	0.239	0.207	0.008	4.963	4.422	4.611	0.788	0.953	0.724	0.112	0.047	0.068
Stip1	0.881	0.796	1.020	3.242	3.266	3.596	0.512	0.796	0.618	0.782	0.982	1.084
Aco1	0.552	0.749	0.828	-0.786	-0.516	-0.534	0.259	0.182	0.349	0.380	0.533	0.629
Angptl2	-2.111	-2.555	-2.927	0.723	0.374	0.386	1.234	1.192	1.164	-0.509	-0.229	-0.178
Vps26a	0.152	0.089	0.254	1.751	1.519	1.930	0.555	0.469	0.374	0.138	0.218	0.267
Mapk3	0.624	0.513	0.653	-4.657	-4.208	-4.279	0.964	0.959	0.817	0.467	0.442	0.546
Hspa4	0.234	0.113	-0.149	3.435	3.715	3.038	0.506	0.345	0.465	0.781	0.646	0.625
Nrp1	-2.310	-2.263	-2.369	-1.381	-1.889	-1.705	1.357	1.433	1.409	-0.505	-0.659	-0.530
Mrc2	0.104	-0.161	0.241	0.746	0.606	0.828	0.964	0.797	0.919	0.111	0.238	0.232
Pgm1	0.496	0.154	0.527	2.111	2.005	2.260	0.557	0.657	0.604	0.449	0.724	0.663
Kpnb1	0.236	0.320	-0.079	-3.110	-3.353	-3.465	0.259	0.115	0.354	0.860	0.707	0.634
Plaa	-2.890	-2.467	-2.434	4.023	3.974	3.936	0.964	0.952	0.991	-0.614	-0.595	-0.828
Ruvbl2	0.146	0.279	0.562	-0.234	-0.418	-0.324	0.569	0.733	0.640	0.141	0.365	0.358
Stag2	0.663	0.241	0.355	5.123	5.495	5.046	0.212	0.262	0.283	0.471	0.815	0.661
Cntn1	0.193	0.558	0.141	-2.345	-2.282	-2.248	0.876	0.968	0.775	0.789	1.022	0.985
Actn1	-2.111	-2.430	-2.262	2.824	2.249	2.551	0.508	0.762	0.553	-0.503	-0.568	-0.758

(Cont'd...)

Table S1. (Continued)

Gene	2D-cultured BMSCs_1	2D-cultured BMSCs_2	2D-cultured BMSCs_3	BO-1d_1	BO-1d_2	BO-1d_3	BO-7d_1	BO-7d_2	BO-7d_3	BO-14d_1	BO-14d_2	BO-14d_3
Iars	0.102	0.337	0.008	3.680	3.652	3.177	0.214	0.295	0.145	0.111	0.028	-0.017
Rtn4	0.601	0.646	0.416	-4.023	-4.193	-3.888	0.788	0.736	0.977	0.416	0.282	0.344
Sfpq	0.237	-0.052	0.677	1.410	1.182	1.785	0.619	0.529	0.678	0.783	0.664	0.564
Megf10	-2.310	-2.444	-2.309	-3.164	-2.551	-2.786	0.259	0.231	0.062	-0.564	-0.295	-0.351
Eif5a	0.128	0.295	-0.209	0.987	1.279	0.907	0.876	0.877	1.096	0.132	0.322	0.332
Kif5b	0.602	0.289	0.560	3.371	4.310	3.723	0.500	0.796	0.499	0.506	0.277	0.389
Serpinf1	0.201	-0.124	-0.013	-3.123	-2.746	-3.077	0.213	0.149	0.228	0.710	0.533	0.678
Htra1	-2.890	-2.534	-2.978	2.702	2.347	2.393	0.964	0.898	1.009	-0.618	-0.310	-0.353
Tll12	0.145	-0.122	0.426	-4.567	-4.320	-4.718	0.498	0.545	0.417	0.131	0.404	0.349
Pgam1	0.565	0.367	0.491	1.357	1.405	0.917	0.208	0.110	0.345	0.494	0.329	0.441
Psmid7	0.261	-0.057	-0.068	4.388	4.046	5.281	0.964	0.930	0.944	0.706	0.734	0.889
Tpr	-3.092	-3.066	-2.908	-2.410	-2.533	-2.928	0.558	0.689	0.679	-0.623	-0.620	-0.555
Anxa2	0.104	-0.233	-0.036	3.286	2.877	2.734	0.234	0.237	0.147	0.122	0.008	0.053
Glg1	0.554	0.291	0.563	0.629	0.543	0.473	0.788	0.802	1.172	0.455	0.492	0.515
Rack1	0.214	0.274	0.197	-0.921	-1.235	-1.356	0.563	0.739	0.748	0.868	0.916	0.885
Ilk	-3.802	-3.552	-3.751	3.567	3.678	3.122	0.230	0.155	0.209	-0.569	-0.844	-0.776

(Contid...)

Table S1. (Continued)

Gene	2D-cultured BMSCs_1	2D-cultured BMSCs_2	2D-cultured BMSCs_3	BO-1d_1	BO-1d_2	BO-1d_3	BO-7d_1	BO-7d_2	BO-7d_3	BO-14d_1	BO-14d_2	BO-14d_3
AheY	0.136	0.073	-0.103	-3.680	-3.518	-2.947	0.876	1.176	0.876	0.110	0.365	0.381
Ywahaq	0.499	0.404	0.353	1.688	1.948	1.965	0.569	0.684	0.573	0.471	0.670	0.505
Actg1	0.233	-0.093	0.079	2.234	2.147	1.985	0.257	0.388	0.182	0.709	1.073	0.959
Adh4	-2.811	-3.270	-3.131	-2.335	-1.862	-2.636	0.788	1.126	0.939	-0.515	-0.860	-0.817
Efemp1	0.154	-0.195	-0.273	0.345	0.233	0.226	0.505	0.679	0.475	0.112	0.438	0.441
Fn1	0.566	0.344	0.638	2.789	2.576	2.486	0.236	0.371	0.167	0.463	0.546	0.422
Mmp2	-2.799	-3.419	-3.509	-0.635	-0.394	-0.319	1.551	1.539	1.369	-0.504	-0.576	-0.489
Thbs1	0.127	0.024	0.391	1.456	1.266	1.042	1.234	1.285	1.364	0.128	0.094	0.213
Anxa1	0.630	0.206	0.888	-1.788	-2.214	-2.112	2.251	1.863	1.894	0.524	0.306	0.390
Gstp1	0.212	0.106	-0.013	2.410	2.646	2.387	1.724	1.788	1.561	0.787	0.533	0.541
Aimp2	-3.435	-2.993	-2.531	-2.310	-2.384	-2.625	1.481	1.195	1.548	-0.569	-0.491	-0.570
Nars	0.128	0.420	-0.186	4.046	4.187	4.388	1.688	1.859	1.697	0.116	0.231	0.143
Hpd	0.512	0.566	0.653	-3.987	-3.704	-4.657	1.896	1.518	1.711	0.505	0.351	0.277
Cand1	0.237	0.231	0.331	1.789	1.447	2.061	1.481	1.339	1.381	0.790	0.801	0.850
Pfn1	-2.799	-2.881	-3.358	2.890	3.009	3.254	1.857	1.623	1.576	-0.505	-0.762	-0.859
Glo1	0.100	0.220	0.362	-1.111	-0.780	-1.145	1.410	1.246	1.315	0.116	0.129	0.199

(Cont'd...)

Table S1. (Continued)

Gene	2D-cultured BMSCs_1	2D-cultured BMSCs_2	2D-cultured BMSCs_3	BO-1d_1	BO-1d_2	BO-1d_3	BO-7d_1	BO-7d_2	BO-7d_3	BO-14d_1	BO-14d_2	BO-14d_3
Agrn	0.682	0.912	0.704	4.321	4.568	4.601	1.086	1.572	1.044	0.509	0.458	0.419
Ppp2r1a	0.283	0.105	0.378	-2.788	-3.086	-2.804	1.351	1.803	2.049	0.781	0.941	0.868
Hhip1l	-3.435	-3.401	-2.984	1.123	1.179	1.170	1.692	1.512	1.656	-0.516	-0.406	-0.520
Mfige8	0.123	0.541	-0.067	2.045	2.060	1.935	1.222	1.234	1.208	0.129	-0.120	-0.059
CXCL12	0.607	0.217	0.514	-4.700	-4.516	-4.073	2.476	1.849	1.860	0.425	0.440	0.615
Prpf19	0.187	0.293	0.249	3.876	4.072	3.540	1.410	1.719	1.557	0.782	0.941	0.867
Coll2a1	-3.421	-3.652	-4.074	0.812	0.799	1.265	1.493	1.197	0.958	-0.617	-0.563	-0.721
Ptprs	0.125	0.172	0.165	-1.345	-1.258	-1.217	2.026	2.022	1.654	0.125	0.216	0.181
Srsf1	0.686	0.823	0.605	4.678	4.484	5.264	1.410	1.620	1.466	0.426	0.177	0.221
Vps26b	0.287	0.299	0.338	-3.068	-2.412	-3.192	1.222	1.497	1.392	0.789	0.597	0.542
Psmbl	-3.092	-3.283	-3.453	1.510	1.617	1.982	2.064	1.796	1.697	-0.568	-0.648	-0.499
Me1	0.127	0.313	0.243	3.570	3.041	3.641	1.379	1.246	1.894	0.121	0.397	0.531
Tpm3	0.559	0.724	0.595	-3.924	-3.128	-3.559	1.111	1.471	1.278	0.471	0.290	0.291
Tpp2	0.234	0.183	0.565	2.123	2.576	2.305	1.688	1.814	1.672	0.861	0.902	0.780
Arpc4	-4.182	-2.966	-2.927	4.657	4.419	3.857	1.551	1.383	1.839	-0.635	-0.624	-0.621
Nutf2	0.116	0.514	-0.105	-2.079	-1.560	-1.993	1.357	0.985	1.375	0.111	0.361	0.401

(Contd...)

Table S1. (Continued)

Gene	2D-cultured BMSCs_1	2D-cultured BMSCs_2	2D-cultured BMSCs_3	BO-1d_1	BO-1d_2	BO-1d_3	BO-7d_1	BO-7d_2	BO-7d_3	BO-14d_1	BO-14d_2	BO-14d_3
Col5a2	0.566	1.007	0.720	2.651	2.645	2.699	2.270	1.934	1.902	0.473	0.164	0.210
Oit3	0.232	0.645	0.176	-3.286	-3.170	-2.752	1.692	1.808	1.562	0.866	0.974	0.921
Rab14	-3.092	-2.562	-3.334	4.168	4.147	3.585	1.111	1.233	1.183	-0.561	-0.630	-0.755
Psmc4	0.121	0.386	0.294	-4.535	-3.480	-3.857	1.351	1.772	1.956	0.126	0.296	0.226
Cct3	0.680	1.003	0.786	1.788	1.691	1.928	1.410	1.529	1.830	0.417	0.293	0.260
Iqgap1	0.231	0.090	0.484	2.702	2.669	2.439	1.086	1.006	1.409	0.784	0.649	0.443
Mtap	-3.110	-3.154	-3.267	-0.868	-0.968	-0.475	1.857	2.068	2.240	-0.564	-0.558	-0.620
Fbln2	0.138	-0.268	0.089	3.680	3.484	3.164	1.551	1.413	1.692	0.113	-0.028	0.007
Pa2g4	0.509	0.587	0.518	-4.046	-3.034	-3.393	1.086	1.275	1.433	0.418	0.336	0.269
Lgals1	0.281	0.501	0.033	4.789	4.554	4.331	2.026	2.182	2.009	0.707	0.759	0.657
Gdi2	-3.779	-2.806	-2.515	-1.011	-0.963	-1.236	2.068	1.647	1.631	-0.625	-0.821	-0.895
Thbs2	0.133	0.136	0.086	2.310	3.209	3.127	1.111	1.098	1.114	0.115	0.273	0.273
Cap1	0.688	0.747	0.580	3.110	3.423	3.111	1.876	1.874	2.266	0.467	0.688	0.782
Asna1	0.187	-0.033	0.062	-2.457	-2.122	-1.888	1.551	1.899	1.418	0.780	0.640	0.615
Lpl	-3.110	-3.795	-3.699	4.508	4.365	4.090	1.000	1.373	1.266	-0.564	-0.762	-0.747
Bgn	0.150	0.404	0.122	2.410	2.738	2.558	1.688	2.155	1.777	0.129	-0.077	-0.161

(Contd...)

Table S1. (Continued)

Gene	2D-cultured BMSCs_1	2D-cultured BMSCs_2	2D-cultured BMSCs_3	BO-1d_1	BO-1d_2	BO-1d_3	BO-7d_1	BO-7d_2	BO-7d_3	BO-14d_1	BO-14d_2	BO-14d_3
Eef1g	0.564	0.840	0.573	-3.570	-3.726	-3.316	1.724	1.726	1.563	0.422	0.714	0.499
Hist1h4b	0.230	0.205	0.006	1.567	1.365	1.330	1.000	1.375	1.210	0.705	0.518	0.430
Arhgdia	-2.811	-3.104	-3.059	2.345	2.096	2.045	2.476	2.068	1.819	-0.509	-0.644	-0.642
Dars	0.136	-0.070	0.093	-4.321	-3.926	-4.437	1.410	1.603	1.722	0.116	0.366	0.347
Rcn1	0.567	0.663	0.557	3.511	4.230	3.363	1.357	1.160	1.192	0.472	0.257	0.276
Dync1h1	0.289	0.138	0.619	-1.602	-1.642	-1.148	2.270	1.896	1.610	0.857	0.802	0.901
Igfb1	-3.110	-3.978	-3.111	3.179	3.162	3.222	1.896	1.369	1.537	-0.568	-0.506	-0.615
App	0.110	0.120	0.347	-2.310	-2.947	-2.413	1.000	1.185	1.405	0.116	0.112	0.121
Notch3	0.618	0.370	0.690	3.435	2.945	2.539	1.688	1.874	1.970	0.520	0.216	0.113
Col3a1	0.278	0.660	0.041	1.841	1.887	2.538	1.551	1.703	1.557	0.864	0.607	0.572
Sema5a	-2.530	-3.511	-3.401	-3.488	-3.423	-3.851	1.234	1.230	1.219	-0.624	-0.592	-0.625
Aldh9a1	0.140	0.363	-0.114	4.456	4.410	4.986	1.857	1.997	1.823	0.135	0.014	-0.024
Eif3m	0.461	0.607	0.656	-1.610	-1.548	-1.916	1.692	1.521	1.880	0.516	0.473	0.385
Fam129b	0.214	0.419	0.195	2.788	2.741	3.441	1.333	1.472	1.432	0.786	0.471	0.381
Eif3k	-3.421	-3.677	-2.870	-2.946	-3.178	-2.543	2.251	1.560	2.034	-0.512	-0.388	-0.395
Eifemp2	0.123	0.130	0.067	1.357	1.156	1.371	2.068	1.609	1.275	0.124	0.414	0.488

(Contd...)

Table S1. (Continued)

Gene	2D-cultured BMSCs_1	2D-cultured BMSCs_2	2D-cultured BMSCs_3	BO-1d_1	BO-1d_2	BO-1d_3	BO-7d_1	BO-7d_2	BO-7d_3	BO-14d_1	BO-14d_2	BO-14d_3
Shmt2	0.460	0.400	0.939	3.567	3.530	4.234	1.000	1.120	1.208	0.518	0.741	0.798
Pfkf	0.232	0.529	0.091	-3.688	-4.275	-4.818	1.501	1.934	1.958	0.789	0.705	0.744
Hspa8	-2.811	-2.569	-2.824	2.457	2.720	2.153	1.254	1.766	1.746	-0.572	-0.392	-0.357
Itga3	0.132	0.163	-0.164	3.678	3.079	3.691	1.333	1.199	1.288	0.141	0.120	0.079
Nid2	0.559	0.488	0.424	-1.724	-1.281	-1.678	2.270	1.639	1.991	0.413	0.349	0.317
Plscr3	0.213	0.479	0.009	4.567	4.327	4.742	1.379	1.662	1.543	0.784	1.188	1.100
Cct4	-3.421	-3.857	-3.651	-2.111	-2.395	-2.163	1.481	1.461	0.946	-0.567	-0.544	-0.574
Col5a1	0.127	0.284	0.337	3.068	2.300	2.945	2.064	1.635	1.744	0.114	0.475	0.512
Coll1a1	0.458	0.612	0.510	0.467	0.518	0.495	3.345	3.101	2.867	1.410	1.759	1.874
Ywhag	0.214	0.592	0.067	-3.435	-2.939	-3.000	1.234	1.300	1.108	0.786	0.804	0.736
Col4a1	-3.092	-2.804	-2.466	4.535	3.370	4.326	2.251	2.071	1.619	-0.623	-0.701	-0.650
Fth1	0.100	0.283	0.163	-1.788	-1.572	-1.612	1.254	1.747	1.373	0.135	-0.003	-0.073
Fstl1	0.558	0.341	0.334	2.456	2.337	2.509	1.357	1.406	1.206	0.413	0.200	0.204
Rbp7	0.207	0.212	0.258	2.788	3.149	2.692	2.476	1.719	2.030	0.778	0.881	0.819
Sec24a	-3.456	-4.046	-3.707	-3.179	-2.952	-2.541	1.379	1.743	1.940	-0.630	-0.442	-0.422
Nt5c2	0.126	0.109	-0.033	4.678	4.660	4.204	1.111	1.209	1.058	0.113	0.351	0.311

(Contd...)

Table S1. (Continued)

Gene	2D-cultured BMSCs_1	2D-cultured BMSCs_2	2D-cultured BMSCs_3	BO-1d_1	BO-1d_2	BO-1d_3	BO-7d_1	BO-7d_2	BO-7d_3	BO-14d_1	BO-14d_2	BO-14d_3
Actn3	0.512	0.810	0.204	1.211	1.454	1.743	1.520	1.753	1.546	0.420	0.749	0.783
Rpl5	0.234	0.066	0.221	-3.802	-3.399	-3.345	1.551	1.676	1.885	0.779	0.793	0.622
Atp5f1b	-3.092	-2.521	-3.650	2.688	2.666	2.608	1.234	1.158	1.243	-0.505	-0.569	-0.499
Lama2	0.129	0.240	0.004	3.876	3.645	4.489	1.857	1.686	2.018	0.125	0.119	0.125
Lgals3bp	0.560	0.703	0.680	-1.510	-1.306	-1.867	1.896	1.612	1.681	0.471	0.548	0.593
Tie1	0.281	0.289	0.206	0.000	-0.254	-0.222	1.111	1.353	1.286	0.866	0.829	0.889
Hnrnpf	-3.456	-3.696	-4.184	3.811	4.409	4.409	2.270	1.747	2.038	-0.510	-0.627	-0.503
Atic	0.120	0.338	-0.064	-2.335	-2.489	-2.408	1.692	1.931	1.552	0.120	0.259	0.178
Hsp90ab1	0.509	0.356	0.477	3.245	2.950	3.225	1.481	0.932	1.133	0.502	0.328	0.338
Ssc5d	0.257	0.067	-0.025	1.610	1.874	2.173	1.688	1.781	2.029	0.867	0.592	0.721
Prpf8	-3.435	-3.792	-2.910	-4.168	-3.817	-3.846	1.410	1.530	1.512	-0.619	-0.594	-0.482
Col6a2	0.148	0.253	0.332	2.310	2.845	2.407	1.111	1.057	0.952	0.135	0.031	-0.050
Plod1	0.631	0.560	0.641	3.310	3.414	3.839	2.026	2.042	1.784	0.462	0.558	0.482
Tagln2	0.259	-0.047	0.284	-1.357	-1.100	-1.300	1.880	1.888	1.532	0.860	0.951	0.862
Tubb5	-3.802	-3.475	-3.480	4.753	4.672	4.890	0.888	1.533	1.242	-0.506	-0.344	-0.292
Ehd2	0.142	-0.263	-0.270	-2.702	-2.274	-2.545	1.688	2.006	2.180	0.112	0.363	0.344

(Contid...)

Table S1. (Continued)

Gene	2D-cultured BMSCs_1	2D-cultured BMSCs_2	2D-cultured BMSCs_3	BO-1d_1	BO-1d_2	BO-1d_3	BO-7d_1	BO-7d_2	BO-7d_3	BO-14d_1	BO-14d_2	BO-14d_3
Ddx5	0.619	0.347	0.817	3.435	2.576	3.367	1.724	1.696	1.439	0.510	0.293	0.200
Coro1c	0.257	0.249	0.586	2.890	3.585	2.529	1.357	1.080	1.217	0.858	0.879	0.833
Lama4	-2.811	-3.285	-3.012	3.588	3.675	3.761	2.064	1.904	1.758	-0.508	-0.608	-0.618
Cp	0.104	0.124	-0.199	-1.701	-1.422	-2.433	1.551	1.736	1.671	0.120	-0.014	0.038
Cacna2d1	0.623	0.690	0.597	4.310	5.177	4.177	1.357	1.197	1.492	0.400	0.249	0.162
Psmc3	0.191	0.462	0.365	-2.688	-3.029	-2.371	2.064	2.225	1.946	0.781	0.489	0.631
Uba1	-3.802	-3.355	-3.747	2.345	1.899	2.209	1.254	1.314	1.658	-0.625	-0.438	-0.413
Ltbp4	0.112	0.127	0.152	3.802	4.043	3.096	1.086	1.374	1.338	0.113	0.387	0.314
Aco7	0.457	0.873	1.053	-3.011	-3.450	-3.018	1.501	1.698	1.837	0.449	0.768	0.719
Tubb6	0.232	0.496	0.612	4.098	3.353	4.022	1.551	1.445	1.671	0.706	0.859	0.843
Lims1	-3.435	-3.158	-3.445	1.987	2.222	2.410	1.357	1.143	1.573	-0.508	-0.501	-0.512
Fermt3	0.154	-0.276	-0.075	3.567	3.694	3.870	2.251	1.955	1.928	0.130	0.006	-0.074
Dnpep	0.687	0.769	0.733	-1.610	-1.588	-1.669	1.254	1.235	1.587	0.502	0.680	0.744
Snrnp200	0.213	0.325	0.282	2.678	2.163	2.328	1.111	1.429	1.185	0.864	0.650	0.637
Pygl	-3.802	-3.583	-3.384	3.410	3.404	4.547	2.270	2.229	1.844	-0.569	-0.356	-0.309
Nsf1c	0.131	-0.241	0.339	-4.657	-4.515	-3.908	1.254	1.537	1.296	0.132	0.096	0.065

(Contd...)

Table S1. (Continued)

Gene	2D-cultured BMSCs_1	2D-cultured BMSCs_2	2D-cultured BMSCs_3	BO-1d_1	BO-1d_2	BO-1d_3	BO-7d_1	BO-7d_2	BO-7d_3	BO-14d_1	BO-14d_2	BO-14d_3
Fbn1	0.618	0.493	0.635	2.234	2.247	2.802	1.086	1.206	1.408	0.492	0.700	0.688
Set	0.190	0.611	0.493	3.345	3.569	3.537	1.520	1.733	1.752	0.862	0.550	0.367
Olfrml2b	-2.811	-3.402	-3.004	-2.567	-2.893	-2.453	1.410	1.454	1.364	-0.505	-0.751	-0.745
Cs	0.1111	0.349	0.040	4.535	3.829	4.246	1.111	1.185	0.961	0.147	0.466	0.509
Eif4a1	0.686	0.271	0.200	-1.480	-1.484	-1.620	1.520	2.043	2.049	0.410	0.752	0.712
Cops2	0.193	0.259	-0.008	3.876	4.124	3.755	2.068	1.933	1.610	0.707	1.024	0.848
Ruvb1l	-3.421	-3.057	-3.870	2.456	2.109	2.724	1.222	1.054	1.201	-0.506	-0.284	-0.332
Cfl1	0.127	0.520	-0.230	4.046	3.714	4.470	1.501	1.838	2.064	0.126	0.358	0.418
Qsox1	0.617	0.410	0.209	-3.987	-3.650	-3.892	1.410	1.481	1.793	0.496	0.425	0.342
Nme1	0.211	0.266	0.194	4.010	4.377	4.510	1.629	1.046	1.096	0.869	0.681	0.475
Lamb2	-2.811	-3.061	-3.238	-1.846	-1.774	-1.541	1.688	2.269	1.597	-0.563	-0.378	-0.416
Ctsd	0.139	0.310	0.089	2.510	3.051	3.490	1.724	1.771	1.271	0.140	-0.133	-0.072
Wdr1	0.462	0.562	0.287	3.570	3.433	2.885	1.086	1.379	1.147	0.412	0.298	0.268
Glul	0.228	0.123	-0.134	-2.890	-2.280	-3.103	1.351	1.626	1.722	0.862	0.846	0.990
Rtcab	-3.421	-2.899	-2.961	4.098	3.825	3.379	1.692	1.338	1.807	-0.511	-0.436	-0.349
Mamdc4	0.112	-0.284	0.395	1.968	2.162	1.735	1.481	1.060	1.177	0.129	0.059	0.008

(Contd...)

Table S1. (Continued)

Gene	2D-cultured BMSCs_1	2D-cultured BMSCs_2	2D-cultured BMSCs_3	BO-1d_1	BO-1d_2	BO-1d_3	BO-7d_1	BO-7d_2	BO-7d_3	BO-14d_1	BO-14d_2	BO-14d_3
Cpe	0.560	0.900	0.379	-3.123	-3.512	-2.795	1.520	2.275	1.666	0.502	0.409	0.385
Cct6a	0.234	0.059	0.109	2.567	2.298	2.258	1.254	1.296	1.557	0.871	0.580	0.550
Nptxr	-3.092	-3.092	-3.505	3.588	3.650	4.007	1.086	1.200	1.148	-0.625	-0.558	-0.522
Thbs3	0.135	-0.012	-0.102	-1.310	-1.352	-1.562	2.251	1.683	2.069	0.115	0.125	0.074
Urod	0.687	0.828	0.397	4.210	4.986	4.738	1.724	1.252	1.412	0.412	0.520	0.578
Nmt1	0.254	0.171	0.194	-2.234	-1.938	-2.442	1.481	0.969	1.619	0.786	0.943	0.946
Ipo5	-3.421	-2.892	-3.622	3.011	3.401	3.182	1.651	2.038	1.915	-0.510	-0.779	-1.056
Numal	0.120	0.078	0.293	2.987	2.650	2.535	1.254	1.376	1.618	0.110	0.278	0.283
Nptx1	0.593	0.772	0.888	-3.567	-3.787	-4.315	0.888	1.091	1.188	0.503	0.575	0.712
Psmc5	0.257	-0.008	0.232	4.234	4.258	3.974	1.688	1.686	2.091	0.789	0.643	0.710
Grn	-2.530	-3.144	-2.498	-1.968	-1.939	-1.646	2.068	1.403	1.376	-0.509	-0.531	-0.564
Rpsa	0.124	0.453	-0.219	2.946	2.702	2.378	1.333	1.495	1.142	0.142	-0.168	-0.205
Aldoa	0.458	0.393	0.986	3.410	3.107	3.653	2.064	1.542	2.050	0.413	0.338	0.309
Ptgn	0.189	0.384	-0.075	-3.711	-4.127	-3.747	1.692	1.504	1.560	0.862	0.593	0.632
Postn	-3.802	-3.488	-3.458	0.801	0.808	0.691	1.357	1.076	1.337	-0.620	-0.648	-0.610
Ltbp1	0.146	0.531	0.126	2.811	3.138	3.564	2.270	1.652	2.129	0.144	0.260	0.127

(Cont'd...)

Table S1. (Continued)

Gene	2D-cultured BMSCs_1	2D-cultured BMSCs_2	2D-cultured BMSCs_3	BO-1d_1	BO-1d_2	BO-1d_3	BO-7d_1	BO-7d_2	BO-7d_3	BO-14d_1	BO-14d_2	BO-14d_3
Col6a1	0.619	0.286	0.300	2.210	2.783	2.514	1.692	1.555	1.712	0.410	0.535	0.503
Atp6v1g1	0.211	0.625	0.274	-2.946	-2.851	-2.468	1.111	1.218	1.244	0.870	0.572	0.671
Arpc3	-3.779	-3.017	-3.851	3.889	4.802	4.129	2.026	1.742	2.264	-0.510	-0.526	-0.530
Tubb4b	0.113	0.139	0.089	-2.186	-2.384	-2.536	1.724	1.748	1.332	0.147	-0.002	0.010
Anxa4	0.656	0.746	0.529	3.408	3.429	3.160	1.333	1.079	1.237	0.498	0.739	0.630
Dpysl2	0.235	0.278	0.639	3.678	3.343	3.396	1.857	1.855	1.854	0.788	0.860	0.887
Pgk1	-3.802	-3.439	-4.230	-2.580	-2.018	-2.825	1.724	1.626	1.391	-0.618	-0.683	-0.831
Sema3a	0.124	-0.182	-0.067	4.789	4.843	4.227	1.222	1.178	1.267	0.108	0.087	0.005
Mdh1	0.727	0.179	0.882	-3.245	-3.183	-3.014	1.351	1.797	2.217	0.502	0.235	0.304
Ext2	0.190	0.478	-0.112	2.123	2.014	2.236	1.880	1.549	1.517	0.702	0.591	0.693
C8b	-3.779	-3.074	-2.672	3.210	3.707	2.862	1.629	1.571	1.376	-0.567	-0.274	-0.209
Col2a1	0.136	0.502	-0.047	3.179	2.873	2.983	1.651	2.102	2.087	0.111	0.172	0.044
Spon1	0.554	0.861	0.556	-3.488	-3.650	-4.042	1.896	1.725	1.519	0.451	0.348	0.174
Xpnp1	0.234	-0.055	0.412	4.508	4.662	4.003	1.111	1.094	1.226	0.786	0.799	0.565
Cc7	-4.182	-3.229	-3.076	-1.678	-1.462	-1.224	1.351	2.073	1.692	-0.512	-0.362	-0.347
Ccdc80	0.128	0.316	0.228	2.921	2.875	3.281	1.692	1.669	1.450	0.126	0.230	0.069

(Contid...)

Table S1. (Continued)

Gene	2D-cultured BMSCs_1	2D-cultured BMSCs_2	2D-cultured BMSCs_3	BO-1d_1	BO-1d_2	BO-1d_3	BO-7d_1	BO-7d_2	BO-7d_3	BO-14d_1	BO-14d_2	BO-14d_3
Pde5a	0.516	0.374	0.272	3.588	3.939	4.481	1.357	1.206	1.185	0.454	0.382	0.287
Igfbp5	0.211	0.372	0.449	-2.210	-2.324	-2.494	2.064	1.706	1.945	0.871	0.544	0.487
Psmid14	-3.092	-3.112	-3.080	4.678	5.103	5.435	1.269	1.322	1.554	-0.624	-0.653	-0.769
Sars	0.118	0.077	0.384	-2.788	-2.637	-2.956	1.493	1.231	1.130	0.123	-0.151	-0.207
Prkar2b	0.534	0.248	0.644	2.789	2.829	3.139	2.064	1.604	1.708	0.502	0.414	0.240
Usp5	0.236	0.290	0.118	3.345	3.035	3.077	1.379	1.913	1.668	0.868	0.765	0.862
C3	-2.799	-3.903	-3.562	-2.987	-2.913	-2.859	1.000	1.477	1.172	-0.510	-0.337	-0.416
Loxl3	0.116	-0.223	0.100	2.079	2.197	1.805	1.857	2.223	1.873	0.115	-0.177	-0.278
Hif1a	0.405	0.376	0.354	0.561	0.617	0.597	3.551	3.854	3.581	3.802	2.845	4.043
Flnb	0.211	-0.034	0.044	-3.678	-3.967	-4.053	1.493	1.359	1.112	0.779	0.913	0.883
Ptges3	-2.811	-2.639	-3.612	4.535	4.043	4.223	1.520	2.001	2.275	-0.511	-0.520	-0.654
Cspg4	0.132	0.202	0.451	-1.111	-1.301	-1.013	1.551	1.537	1.891	0.118	-0.069	-0.089
Tuba4a	0.544	0.844	0.469	2.824	2.573	3.213	1.111	1.155	1.180	0.459	0.677	0.713
Hgf	0.215	0.476	0.236	3.410	3.997	4.083	2.476	2.219	1.594	0.788	0.496	0.537
Capzb	-3.456	-4.134	-4.088	-2.789	-3.048	-2.567	1.724	1.477	1.551	-0.510	-0.253	-0.321
Dnm1l	0.122	-0.103	0.061	4.678	4.285	5.303	1.234	1.394	1.068	0.145	-0.077	-0.281

(Contid...)

Table S1. (Continued)

Gene	2D-cultured BMSCs_1	2D-cultured BMSCs_2	2D-cultured BMSCs_3	BO-1d_1	BO-1d_2	BO-1d_3	BO-7d_1	BO-7d_2	BO-7d_3	BO-14d_1	BO-14d_2	BO-14d_3
Cops3	0.634	0.689	0.170	-1.567	-1.432	-1.771	1.501	1.769	2.134	0.456	0.639	0.694
Pygb	0.257	0.626	0.187	2.688	2.531	3.028	1.880	1.337	1.706	0.789	0.895	0.766
Parvb	-3.092	-3.209	-2.849	2.811	3.348	3.055	1.111	1.205	1.282	-0.567	-0.483	-0.443
Lrrc17	0.124	0.149	0.362	-3.345	-3.712	-3.927	1.351	1.582	1.689	0.111	0.469	0.193
Bhmt	0.688	0.160	0.546	4.657	3.943	4.254	1.880	1.527	1.518	0.454	0.554	0.652
Ehd4	0.186	-0.118	0.258	-1.911	-2.673	-1.872	0.987	1.279	1.067	0.868	0.698	0.744
Usp7	-3.421	-3.006	-4.230	4.046	4.165	4.377	1.688	2.153	1.834	-0.567	-0.284	-0.487
Klcl	0.129	0.100	0.348	3.179	3.206	2.819	1.567	1.429	1.382	0.111	0.184	0.263
Clqtntf6	0.595	0.606	0.838	4.386	4.454	3.694	1.111	0.942	1.505	0.410	0.383	0.403
Cyfp1	0.234	-0.101	0.185	-4.098	-4.861	-4.199	1.857	1.881	1.830	0.791	1.084	0.815
Lamb1	-3.779	-3.529	-3.353	2.210	2.280	2.057	1.724	1.823	1.439	-0.567	-0.789	-0.810
Ywhaz	0.120	-0.194	0.280	3.567	3.618	3.896	1.629	1.340	1.316	0.135	0.187	0.163
Tln1	0.448	0.433	0.992	-2.824	-2.323	-3.220	1.651	1.807	1.957	0.458	0.359	0.363
Ncl	0.188	0.332	0.627	4.321	4.446	4.191	1.692	1.463	1.423	0.872	1.011	1.236
Tubala	-3.802	-2.874	-3.737	-3.435	-2.962	-3.393	1.234	1.470	1.079	-0.567	-0.481	-0.453
Tgfb1	0.107	-0.032	0.007	2.946	2.914	3.342	1.688	1.711	2.135	0.111	-0.073	-0.245

(Cont'd...)

Table S1. (Continued)

Gene	2D-cultured BMSCs_1	2D-cultured BMSCs_2	2D-cultured BMSCs_3	BO-1d_1	BO-1d_2	BO-1d_3	BO-7d_1	BO-7d_2	BO-7d_3	BO-14d_1	BO-14d_2	BO-14d_3
Idh2	0.493	0.405	0.443	3.789	3.208	3.937	1.254	1.594	1.895	0.501	0.381	0.284
Cops8	0.232	0.521	-0.148	-2.186	-2.350	-2.015	1.111	1.241	1.286	0.789	0.722	0.872
Cct8	-2.811	-3.809	-3.128	4.535	3.816	4.943	2.270	2.058	1.706	-0.510	-0.409	-0.276
Phl1	0.130	0.117	0.523	2.921	3.540	2.796	1.379	1.594	1.261	0.111	-0.009	0.035
Capza2	0.561	0.484	0.677	-2.890	-2.480	-2.965	1.222	1.286	1.197	0.505	0.381	0.511
Ipo7	0.231	0.675	0.073	3.310	3.401	3.915	2.064	1.656	2.196	0.791	0.786	0.497
Hnrnpu	-3.802	-3.075	-3.692	3.286	3.402	2.867	1.896	1.693	1.457	-0.624	-0.732	-0.840
Uso1	0.163	0.329	-0.009	-3.110	-3.007	-3.166	1.333	1.265	1.169	0.133	0.317	0.076
Lamc1	0.607	0.288	0.340	3.688	3.350	4.710	1.520	1.749	1.986	0.410	0.330	0.284
Dnajb11	0.202	0.115	0.021	3.924	4.073	3.704	1.254	1.637	1.601	0.710	0.876	0.737
Prss23	-3.123	-3.644	-2.877	-1.610	-1.964	-1.900	1.222	1.267	1.308	-0.624	-0.739	-0.807
Pcbp2	0.116	-0.189	-0.172	3.876	3.247	3.803	2.026	1.722	1.682	0.111	-0.133	-0.170
Rplp0	0.559	0.649	0.870	2.789	2.544	2.572	1.724	1.689	1.601	0.406	0.256	0.406
Ext1	0.261	0.006	0.213	3.011	3.368	3.272	1.357	1.223	1.552	0.714	1.168	0.994
Vat1	-3.802	-4.167	-3.400	-2.946	-2.051	-2.770	2.476	1.762	2.156	-0.624	-0.691	-0.644
Igf2	0.155	0.257	0.470	3.811	4.255	3.539	1.269	1.334	1.397	0.139	0.213	0.305
Emilin1	0.460	0.385	0.532	-1.567	-1.935	-1.303	1.629	1.103	1.340	0.502	0.582	0.633

(Cont'd..)

Table S1. (Continued)

Gene	2D-cultured BMSCs_1	2D-cultured BMSCs_2	2D-cultured BMSCs_3	BO-1d_1	BO-1d_2	BO-1d_3	BO-7d_1	BO-7d_2	BO-7d_3	BO-14d_1	BO-14d_2	BO-14d_3
Hsp90aa1	0.233	-0.051	0.575	3.678	4.061	3.182	2.064	1.933	1.713	0.792	0.903	0.943
Acta2	-2.811	-3.452	-2.744	2.890	3.080	2.381	1.128	1.746	1.382	-0.624	-0.243	-0.279
Hgd	0.118	0.511	0.438	-4.386	-4.179	-4.726	1.493	1.524	1.072	0.146	-0.039	-0.049
F13a1	0.563	0.465	0.901	5.024	4.924	5.077	1.857	1.708	1.594	0.407	0.174	0.127
Rap1b	0.234	0.171	0.593	-1.111	-1.601	-1.344	1.724	1.279	1.364	0.789	0.519	0.397
Sparc	-3.456	-3.303	-4.028	2.811	3.596	2.727	1.629	1.068	1.434	-0.510	-0.319	-0.239
Pxdn	0.122	0.234	-0.025	2.702	2.740	2.380	1.651	1.944	1.675	0.138	0.234	0.257
Bmp1	0.509	0.696	0.283	3.789	3.599	3.396	1.896	1.577	1.288	0.410	0.166	0.155
Psmc6	0.236	-0.106	0.540	-2.345	-2.686	-2.728	0.987	1.098	1.192	0.862	0.717	0.631
Impdh2	-3.435	-2.570	-2.915	4.123	3.724	4.409	1.857	2.078	1.982	-0.507	-0.311	-0.290
Vcan	0.115	0.294	-0.224	-1.510	-1.759	-1.601	1.724	1.656	1.637	0.134	0.223	0.156
Matn2	0.624	0.446	0.776	3.924	3.914	4.126	1.481	0.960	1.013	0.456	0.239	0.292
Ctsb	0.257	-0.044	0.404	2.987	2.864	3.458	1.520	1.841	1.889	0.868	0.876	0.937
Ran	-3.802	-3.732	-3.008	-2.601	-3.509	-2.525	1.410	1.266	1.533	-0.620	-0.250	-0.221
Sec24c	0.135	0.140	-0.125	3.456	3.595	3.102	1.357	0.940	1.450	0.108	-0.129	-0.219
Vcam1	0.624	0.875	0.540	-0.121	-0.123	0.422	1.254	1.543	1.797	0.456	0.257	0.397

(Contd...)

Table S1. (Continued)

Gene	2D-cultured BMSCs_1	2D-cultured BMSCs_2	2D-cultured BMSCs_3	BO-1d_1	BO-1d_2	BO-1d_3	BO-7d_1	BO-7d_2	BO-7d_3	BO-14d_1	BO-14d_2	BO-14d_3
Bglap	0.215	-0.059	-0.018	0.793	0.670	0.480	1.493	1.427	1.299	2.921	3.507	3.571
Bmp2	-3.092	-3.516	-3.087	3.068	2.941	2.513	1.857	1.711	1.773	-0.568	-0.289	-0.175
Dmp1	0.138	-0.158	0.538	3.876	4.639	3.130	1.880	1.519	1.385	0.129	-0.079	-0.105
Runx2	0.510	0.496	0.813	0.456	0.741	0.674	0.987	1.124	1.147	4.508	3.983	4.338
Spp1	0.211	0.374	0.254	2.824	2.477	2.814	1.520	2.043	1.975	0.868	0.578	0.569
Wnt10b	-3.802	-4.060	-2.885	3.435	2.518	3.417	1.692	1.830	1.407	-0.512	-0.788	-0.668
Gapdh	0.112	0.442	0.124	3.286	2.705	3.038	1.222	1.195	1.565	0.129	-0.127	-0.262
Angpt1	0.561	0.195	0.435	-0.113	-0.020	-0.151	2.068	1.563	1.452	0.411	0.489	0.419
Tie2	0.187	0.431	0.085	0.194	0.265	-0.265	1.481	1.318	1.031	0.873	0.879	0.804
Vegfa	-3.092	-3.735	-2.841	0.121	0.133	0.382	1.896	1.645	1.515	1.940	3.110	3.065
Cdh1	0.142	0.111	0.257	3.678	3.737	3.391	1.857	1.962	1.730	0.123	0.184	0.167
Pdgfra	0.656	0.800	0.208	3.011	3.592	2.947	1.567	1.825	1.290	0.497	0.276	0.394