

Figure S1 related to Figure 1

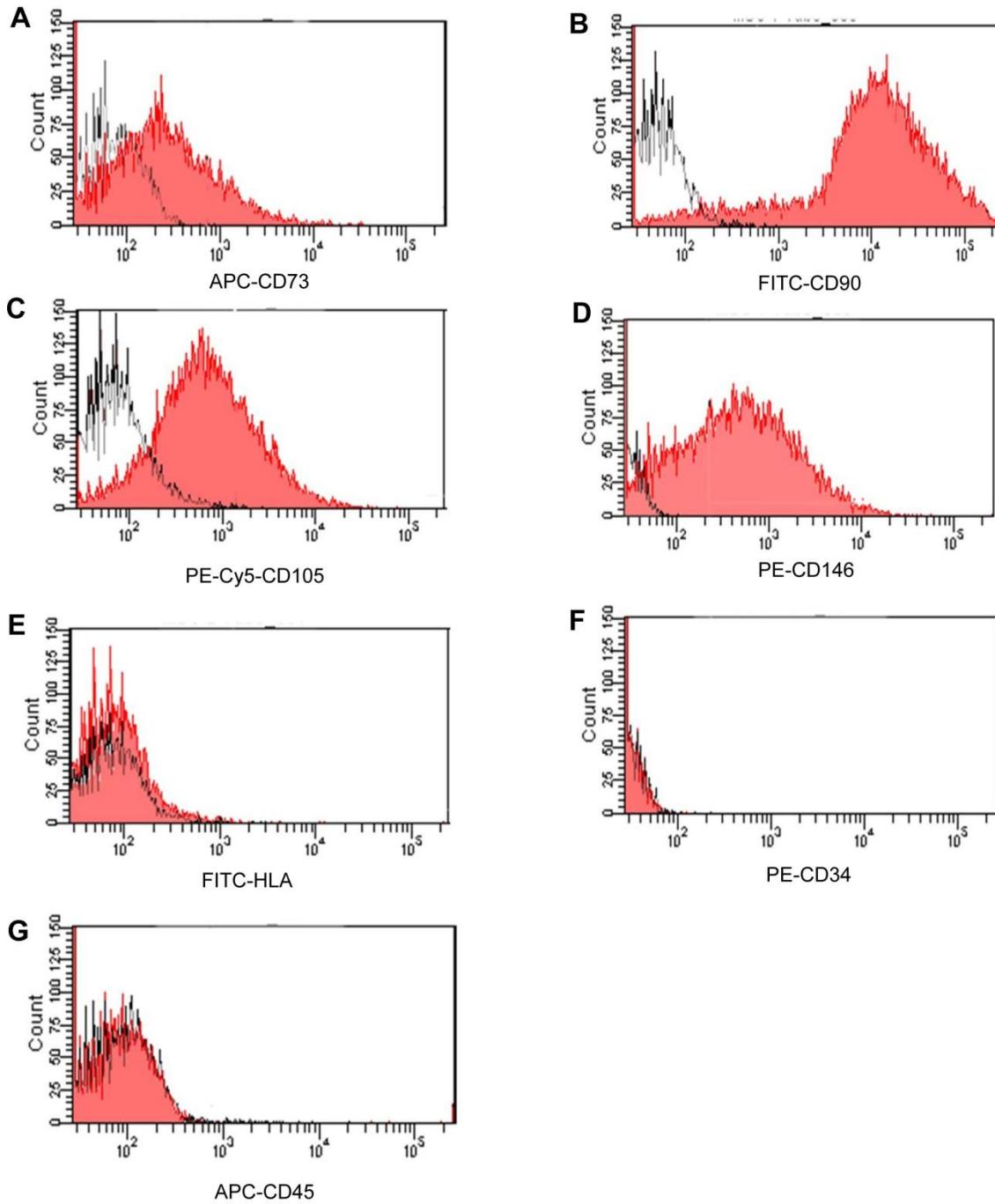


Figure S1. Characterization of human MSC surface markers by flow cytometry (Related to Figure 1). (A-D) MSCs expressed CD73, CD90, CD105 and CD146, respectively. (E-G) MSCs did not express CD34, CD45 and HLA, respectively.

Fig. S2 related to Figure. 2

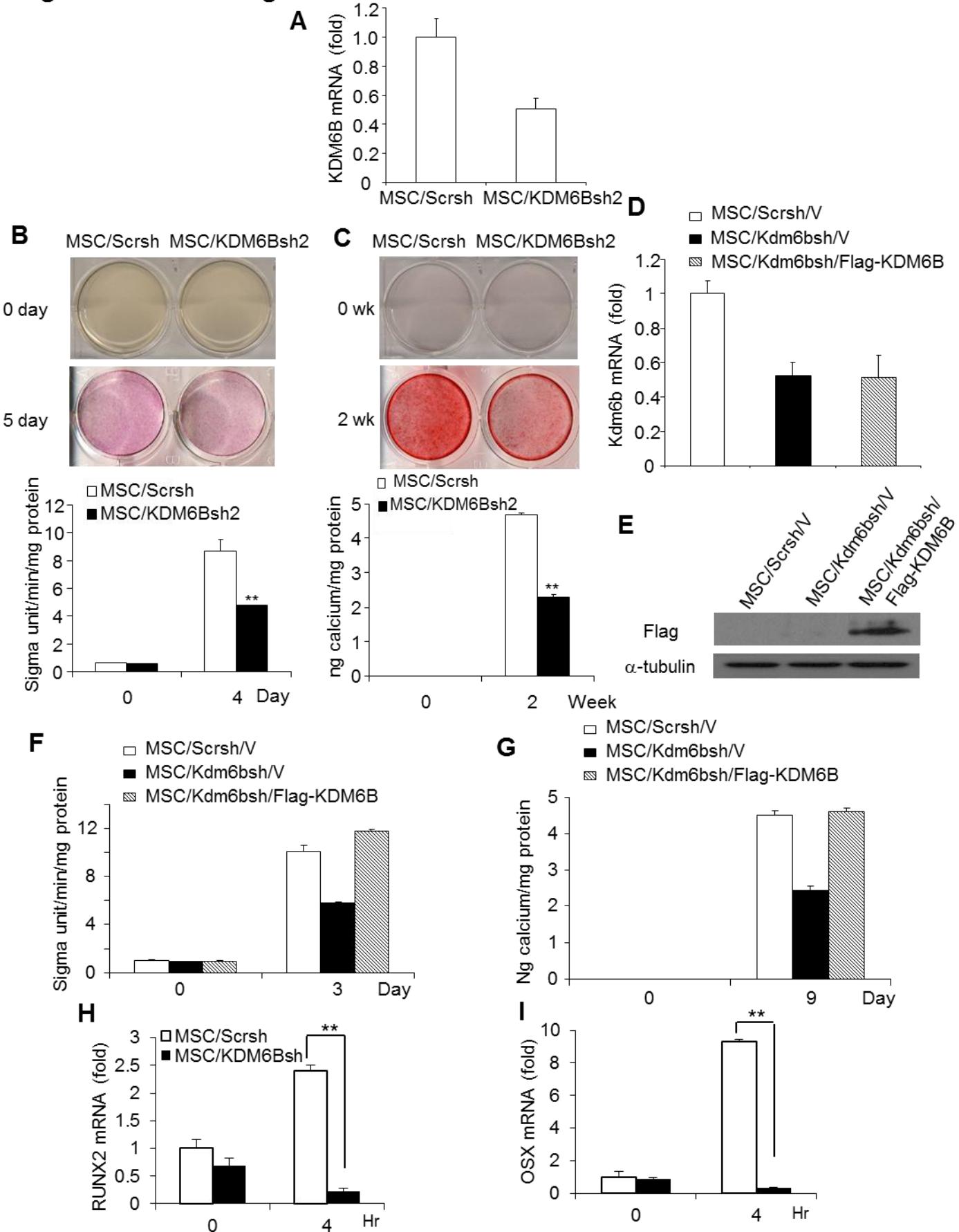


Figure S2. KDM6B is required for osteogenic differentiation of MSCs (Related to Figure 2). (A) Knock-down of *KDM6B* by a different shRNA sequence as determined by Real-time RT-PCR. MSC/KDM6Bsh2, MSCs expressing KDM6B shRNA2; MSC/Scrsh, MSCs expressing scramble shRNA. (B) Knock-down of KDM6B inhibited ALP activities in MSCs. Values are mean \pm s.d for triplicate samples from a representative experiment. **P < 0.01. (C) Knock-down of KDM6B inhibited mineralization in MSCs. **P < 0.01. (D) Examination of *Kdm6b* mRNA by Real-time RT-PCR. *Kdm6b* in mouse MSCs were knocked down and subsequently transduced with retroviruses expressing human Flag-KDM6B. MSC/Srcsh/V, MSC/Scrsh expressing empty vector; MSC/Kdm6bsh/V, MSC/Kdm6bsh expressing empty vector; MSC/Kdm6bsh/Flag-KDM6B, MSC/Kdm6bsh expressing human Flag-KDM6B. (E) The restoration of KDM6B in *Kdm6b* knock-down MSCs by Western blot analysis. (F) The restoration of *KDM6B* in MSC increased ALP activities. (G) The restoration of *KDM6B* in MSCs increased mineralization. (H) Knock-down of KDM6B inhibited BMP-induced *Runx2* expression as determined by Real-time RT-PCR. (I) Knock-down of KDM6B inhibited BMP-induced *OSX* expression as determined by Real-time RT-PCR. .

Figure S3 related to Figure. 3

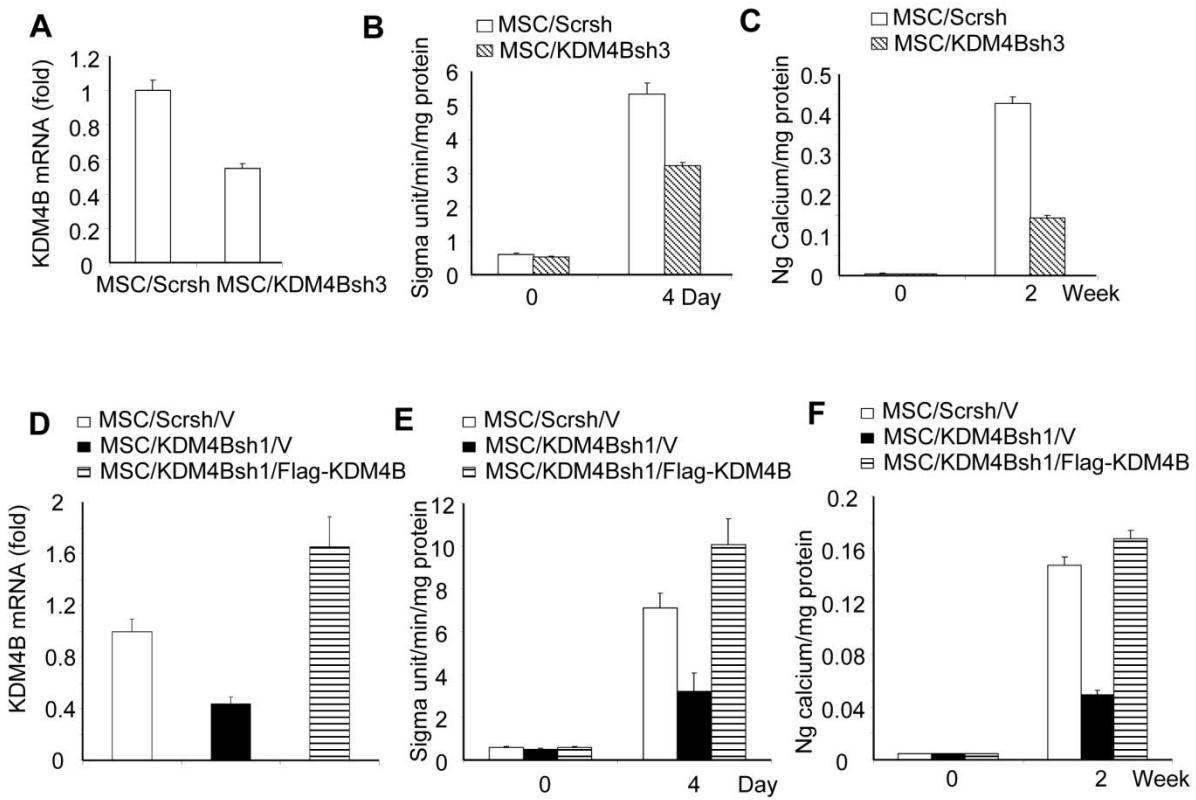


Figure S3. KDM4B is required for osteogenic differentiation of MSCs (Related to Figure 3).

(A) Knock-down of *KDM4B* by a different shRNA sequence as determined by Real-time RT-PCR. MSC/KDM4Bsh3, MSCs expressing KDM4B shRNA3; MSC/Scrsh, MSCs expressing scramble shRNA. (B) Knock-down of *KDM4B* inhibited ALP activities in MSCs. **P < 0.01. (C) Knock-down of *KDM4B* inhibited mineralization in MSCs. **P < 0.01. (D) The restoration of KDM4B expression in KDM4B knock-down MSCs as determined by Real-time RT-PCR. MSC/Srcsh/V, MSC/Scrsh expressing empty vector; MSC/KDM4Bsh1/V, MSC/KDM4Bsh1 expressing empty vector; MSC/KDM4Bsh1/Flag-KDM6B, MSC/KDM4Bsh1 expressing human Flag-KDM6B. (E) The restoration of KDM4B in MSC increased ALP activities. (F) The restoration of KDM4B in MSCs increased mineralization.

Figure S4 related to Figure 5

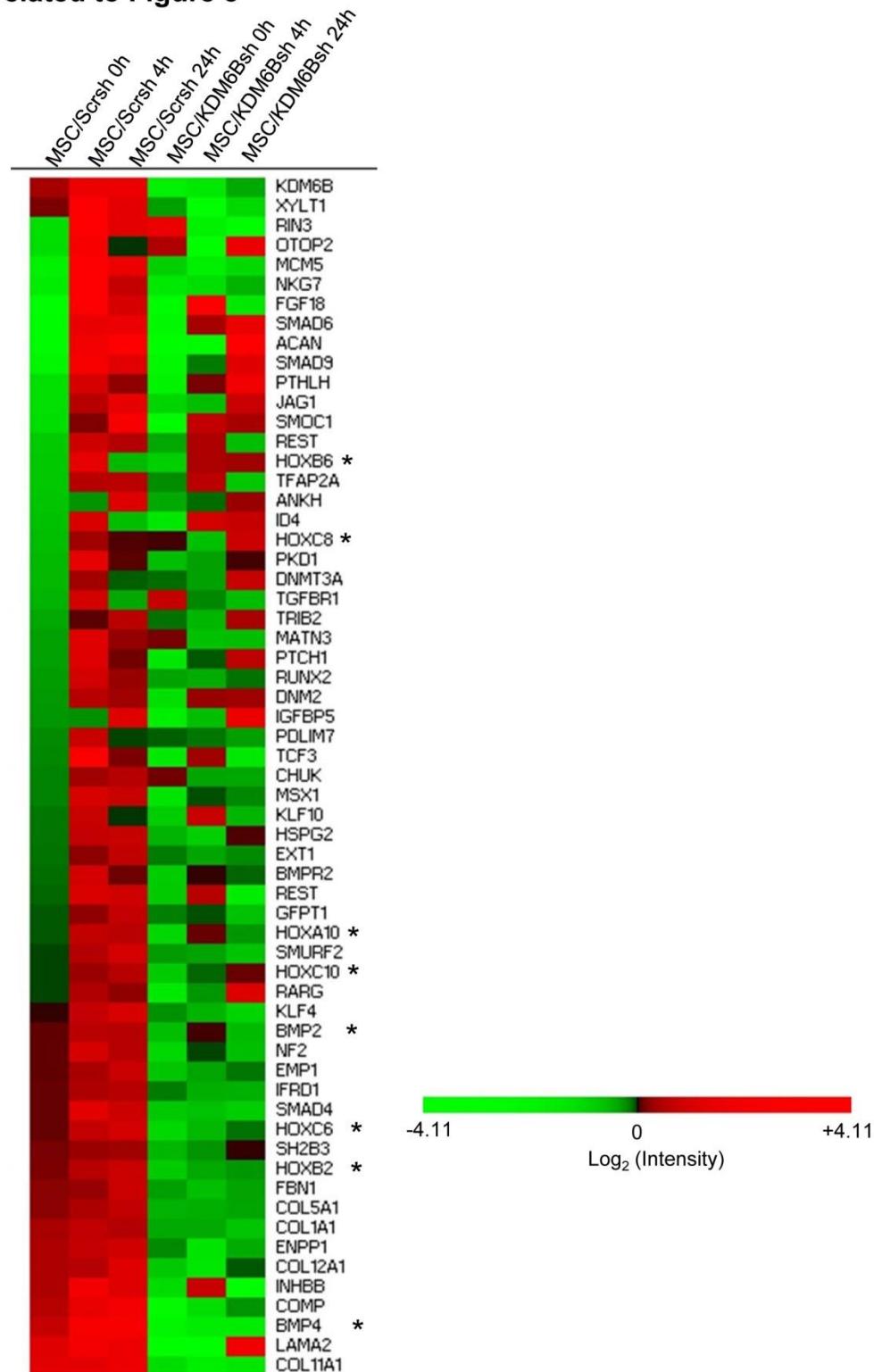


Figure S4. Global analysis of KDM6B-dependent genes by microarray (Related to Figure 5). The heatmap of representative KDM6B-dependent genes induced by BMPs at 0, 4 and 24 hr.

Figure S5 related to Figure. 5

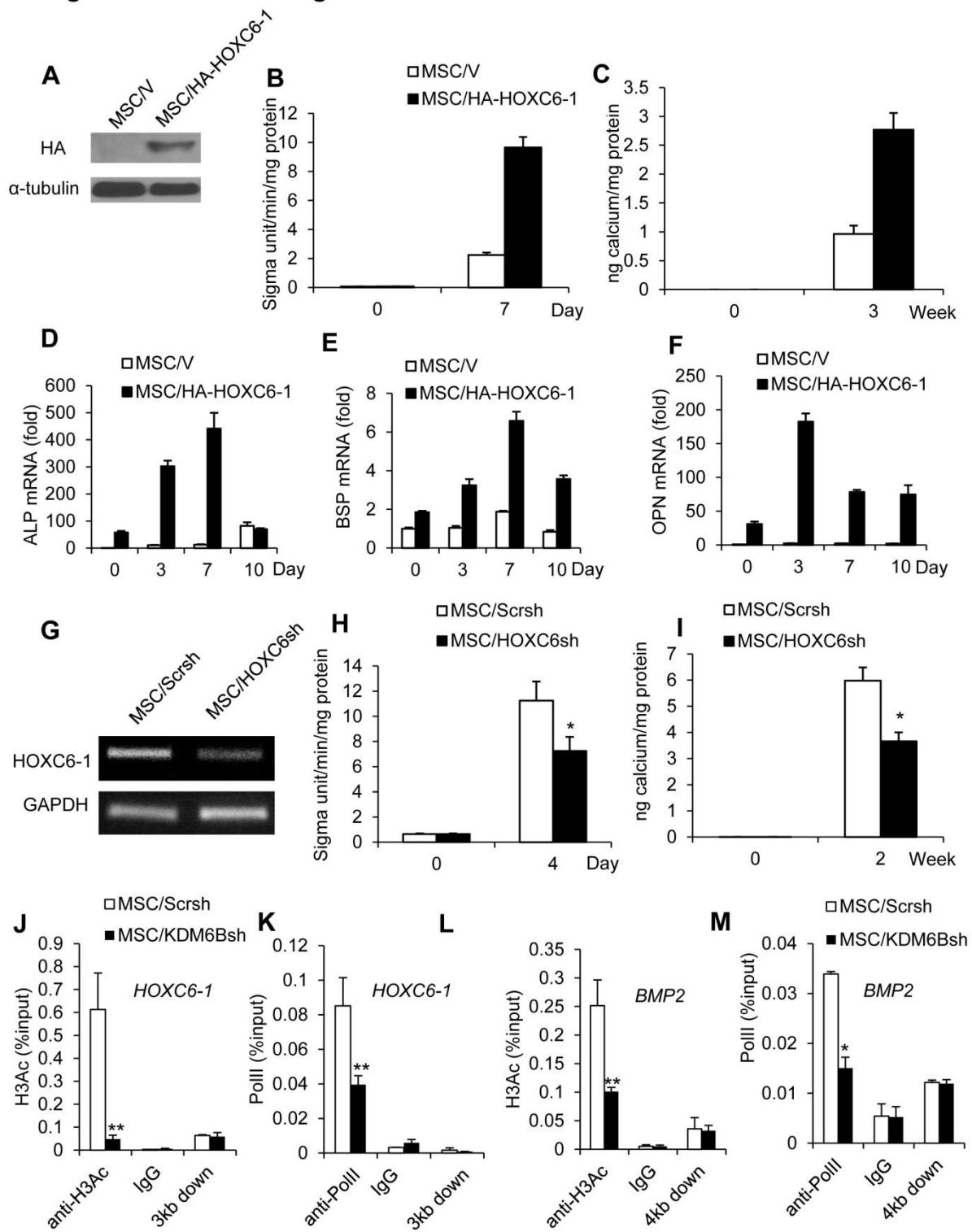


Figure S5. HOXC6-1 plays a functional role in osteogenic differentiation of MSCs

(Related to Figure 5). (A) Over-expression of HOXC6-1 in MSCs. (B) Over-expression of HOXC6-1 increased ALP activities in MSCs. (C) Over-expression of HOXC6-1 increased mineralization in MSCs. (D) Over-expression of HOXC6-1 enhanced ALP expression. (E) Over-expression of HOXC6-1 enhanced *BSP* expression (F) Over-expression of HOXC6-1 enhanced *OPN* expression. (G) The knock-down of *HOXC6-1* in MSCs by shRNA. (H) The knock-down of *HOXC6-1* attenuated ALP activities in MSCs. (I) The knock-down of *HOXC6-1* attenuated mineralization in MSCs. (J) The knock-down of KDM6B reduced H3 acetylation on the HOXC6-1 promoter. (K) The knock-down of KDM6B reduced the recruitment of Pol II to the HOXC6-1 promoter. (L) The knock-down of KDM6B reduced H3 acetylation on the BMP2 promoter. (M) The knock-down of KDM6B reduced the recruitment of Pol II to the BMP2 promoter.

Figure S6 related to Figure 6

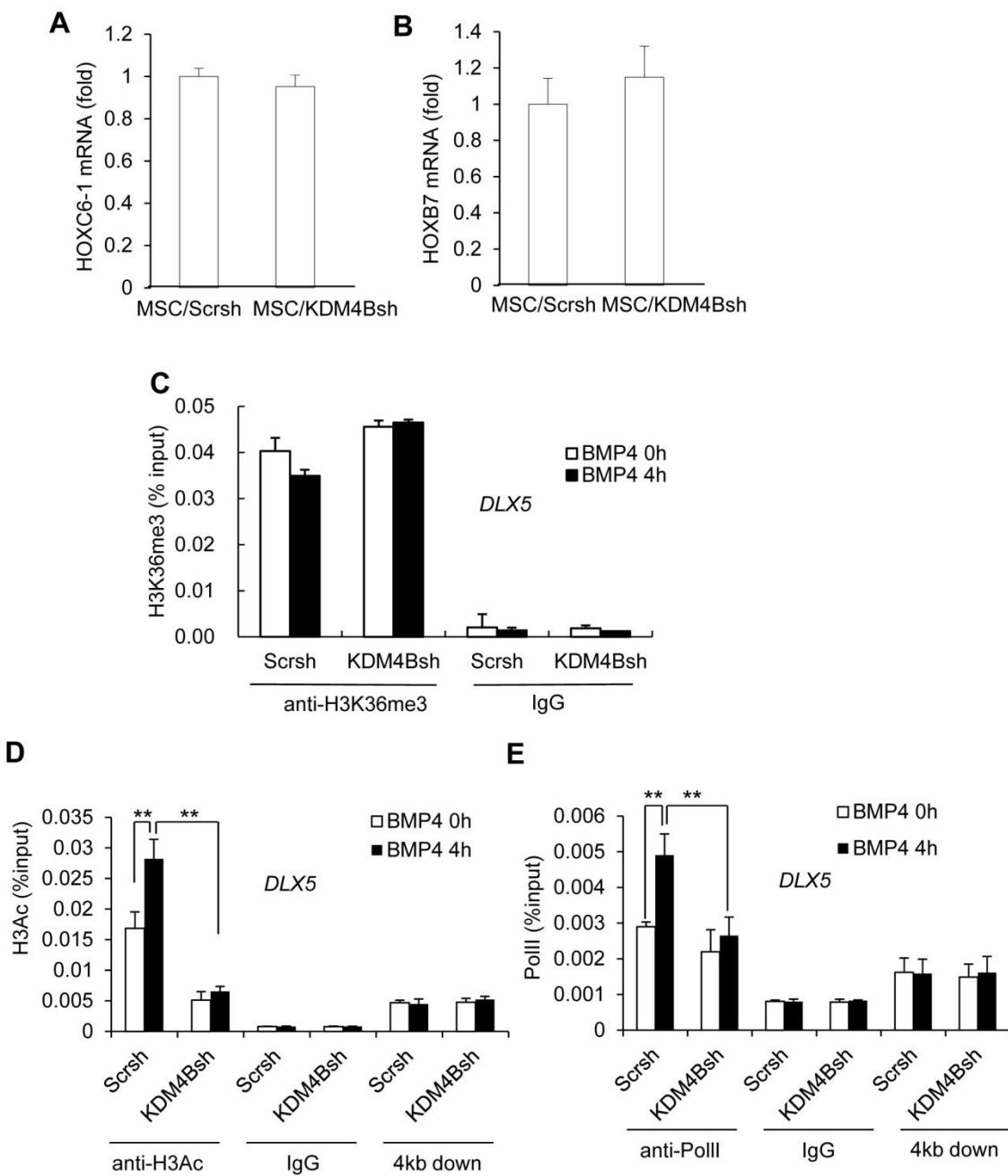


Figure S6. The demethylation of H3K9me3 by KDM4B promotes H3 acetylation and recruits RNA polymerase II (Pol II) to the target gene promoters (Related to Figure 6). (A) The knock-down of *KDM4B* did not affect the expression of *HOXC6-1* by Real-time RT-PCR. (B) The knock-down of *KDM4B* did not affect the expression of *HOXB7* by Real-time RT-PCR. (C) The knock-down of *KDM4B* did not affect H3K36me3 on the *DLX5* promoter. (D) The knock-down of *KDM4B* reduced H3 acetylation on the *DLX5* promoter. (E) The knock-down of *KDM4B* reduced the recruitment of Pol II to the *DLX5* promoter.

Figure S7 related to Figure 6

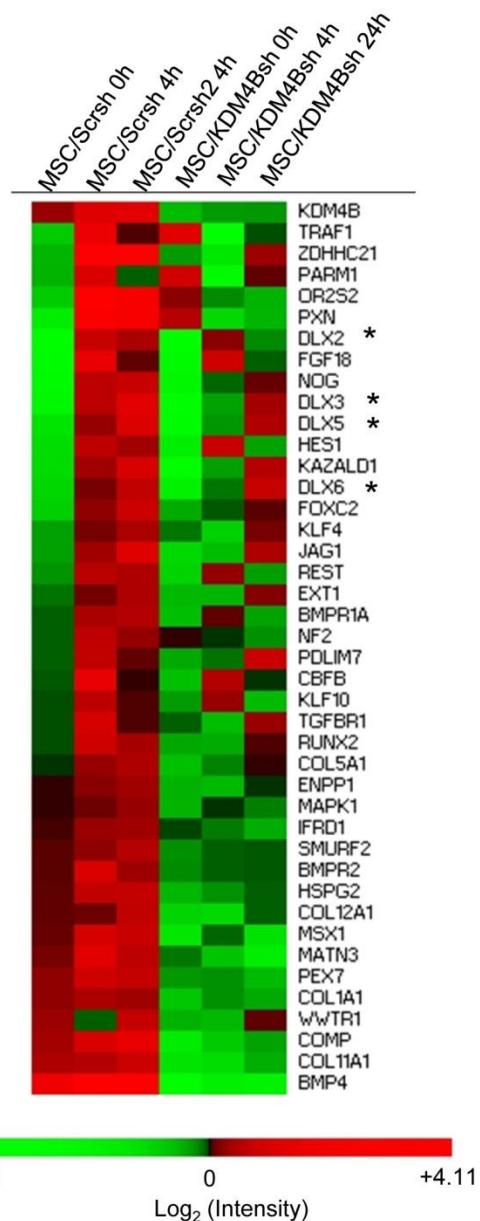


Figure S7. Global analysis of KDM4B-dependent genes by microarray (Related to Figure 6). The heatmap of representative KDM4B-dependent genes induced by BMPs at 0, 4 and 24 hr.

Table S1. GO Analysis of KDM6B-dependent Genes at Basal Level (Related to Figure 5). GO analysis was performed using the online Database for Annotation, Visualization and Integration Discovery (DAVID) Bioinformatics Resources v6.7. P values were calculated based on hypergeometric distribution. Only significantly overexpressed ($p<0.05$) GO terms were included.

Table S2. GO analysis of KDM6B-dependent genes induced by BMP4/7 at 4hr (Related to Figure 5)

GO Term	Count	P Value
GO:0010605-negative regulation of macromolecule metabolic process	37	0.00199
GO:0010604-positive regulation of macromolecule metabolic process	35	0.0492
GO:0009890-negative regulation of biosynthetic process	32	8.84E-04
GO:0031327-negative regulation of cellular biosynthetic process	32	6.18E-04
GO:0006357-regulation of transcription from RNA polymerase II promoter	31	0.04059
GO:0010558-negative regulation of macromolecule biosynthetic process	31	8.64E-04
GO:0009891-positive regulation of biosynthetic process	30	0.03892
GO:0031328-positive regulation of cellular biosynthetic process	30	0.03375
GO:0010557-positive regulation of macromolecule biosynthetic process	30	0.0196
GO:0051172-negative regulation of nitrogen compound metabolic process	30	7.91E-04
GO:0006468-protein amino acid phosphorylation	29	0.03864
GO:0046907-intracellular transport	29	0.03338
GO:0045934-negative regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	29	0.00132
GO:0001501-skeletal system development	29	2.77E-07
GO:0010628-positive regulation of gene expression	28	0.01372
GO:0045935-positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	27	0.04908
GO:0045941-positive regulation of transcription	27	0.01691
GO:0010629-negative regulation of gene expression	27	0.00423
GO:0016481-negative regulation of transcription	25	0.00501
GO:0007010-cytoskeleton organization	23	0.01052
GO:0045893-positive regulation of transcription, DNA-dependent	22	0.04505
GO:0032989-cellular component morphogenesis	19	0.04856
GO:0045944-positive regulation of transcription from RNA polymerase II promoter	19	0.02801
GO:0051253-negative regulation of RNA metabolic process	19	0.02266
GO:0048598-embryonic morphogenesis	19	0.00459
GO:0045892-negative regulation of transcription, DNA-dependent	18	0.03608
GO:0007167-enzyme linked receptor protein signaling pathway	18	0.0259
GO:0009792-embryonic development ending in birth or egg hatching	18	0.02094
GO:0043009-chordate embryonic development	18	0.01961
GO:0007507-heart development	17	6.66E-04
GO:0016568-chromatin modification	15	0.03345
GO:0007389-pattern specification process	15	0.02777
GO:0034660-ncRNA metabolic process	13	0.0411
GO:0045597-positive regulation of cell differentiation	13	0.03983
GO:0030036-actin cytoskeleton organization	13	0.0366
GO:0048729-tissue morphogenesis	13	0.00729
GO:0048705-skeletal system morphogenesis	13	1.16E-04
GO:0007178-transmembrane receptor protein serine/threonine kinase signaling pathway	13	5.11E-05
GO:0003002-regionalization	12	0.03258
GO:0048568-embryonic organ development	11	0.03186
GO:0045165-cell fate commitment	11	0.00827
GO:0022604-regulation of cell morphogenesis	11	0.0055
GO:0051216-cartilage development	11	6.06E-05
GO:0048562-embryonic organ morphogenesis	10	0.01724
GO:0060348-bone development	10	0.01075
GO:0001503-ossification	10	0.00705
GO:0016055-Wnt receptor signaling pathway	9	0.0438
GO:0017038-protein import	9	0.04064
GO:0001655-urogenital system development	9	0.01628
GO:0030198-extracellular matrix organization	9	0.01191
GO:0001822-kidney development	9	0.0075
GO:0030509-BMP signaling pathway	9	3.80E-05
GO:0048706-embryonic skeletal system development	8	0.00763
GO:0031344-regulation of cell projection organization	7	0.04813
GO:0030278-regulation of ossification	7	0.02774
GO:0003007-heart morphogenesis	7	0.02076
GO:0006839-mitochondrial transport	7	0.01612
GO:0042476-odontogenesis	7	0.00502
GO:0001764-neuron migration	6	0.04053
GO:0007179-transforming growth factor beta receptor signaling pathway	6	0.0319
GO:0048704-embryonic skeletal system morphogenesis	6	0.02626
GO:0009612-response to mechanical stimulus	6	0.02453
GO:0030199-collagen fibril organization	6	0.00146
GO:0002274-myeloid leukocyte activation	5	0.04638
GO:0045667-regulation of osteoblast differentiation	5	0.03755
GO:0042475-odontogenesis of dentine-containing tooth	5	0.02742
GO:0006626-protein targeting to mitochondrion	5	0.01733
GO:0070585-protein localization in mitochondrion	5	0.01733
GO:0070167-regulation of biomineral formation	5	0.01407
GO:0030500-regulation of bone mineralization	5	0.01123
GO:0045669-positive regulation of osteoblast differentiation	5	0.00582
GO:0060393-regulation of pathway-restricted SMAD protein phosphorylation	5	0.00132
GO:0031032-actomyosin structure organization	4	0.04868
GO:0050994-regulation of lipid catabolic process	4	0.04033
GO:0045778-positive regulation of ossification	4	0.03278
GO:0060349-bone morphogenesis	4	0.02013
GO:0001502-cartilage condensation	4	0.01749
GO:0002062-chondrocyte differentiation	4	0.01505
GO:0060350-endochondral bone morphogenesis	4	0.01079
GO:0010862-positive regulation of pathway-restricted SMAD protein phosphorylation	4	0.00733
GO:0001958-endochondral ossification	4	0.00463
GO:0030520-estrogen receptor signaling pathway	3	0.04021
GO:0033158-regulation of protein import into nucleus, translocation	3	0.02736
GO:0002063-chondrocyte development	3	0.0166
GO:0002011-morphogenesis of an epithelial sheet	3	0.0166
GO:0033160-positive regulation of protein import into nucleus, translocation	3	0.0166
GO:0060391-positive regulation of SMAD protein nuclear translocation	3	0.01209
GO:0060390-regulation of SMAD protein nuclear translocation	3	0.01209

Table S3. GO analysis of KDM6B-dependent genes induced by BMP4/7 at 24hr (Related to Figure 5)

GO Term	Count	PValue
GO:0006796-phosphate metabolic process	34	0.0250278
GO:0006793-phosphorus metabolic process	34	0.0250278
GO:0042127-regulation of cell proliferation	32	0.0040548
GO:0016310-phosphorylation	31	0.0090636
GO:0008104-protein localization	30	0.0479707
GO:0010605-negative regulation of macromolecule metabolic process	29	0.0092455
GO:0006468-protein amino acid phosphorylation	28	0.0049345
GO:0045184-establishment of protein localization	27	0.0454356
GO:0015031-protein transport	27	0.0411137
GO:0016265-death	27	0.023494
GO:0008219-cell death	26	0.0368797
GO:0007155-cell adhesion	25	0.047497
GO:0022610-biological adhesion	25	0.0465679
GO:0012501-programmed cell death	23	0.0352457
GO:0006915-apoptosis	23	0.0307612
GO:0009890-negative regulation of biosynthetic process	23	0.0187275
GO:0031327-negative regulation of cellular biosynthetic process	23	0.0150366
GO:0010558-negative regulation of macromolecule biosynthetic process	22	0.0213878
GO:0051172-negative regulation of nitrogen compound metabolic process	21	0.0235988
GO:0045934-negative regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	20	0.0374425
GO:0019220-regulation of phosphate metabolic process	20	0.0232554
GO:0051174-regulation of phosphorus metabolic process	20	0.0232554
GO:0042325-regulation of phosphorylation	20	0.0160385
GO:0001501-skeletal system development	20	2.34E-04
GO:0007010-cytoskeleton organization	18	0.0320505
GO:0051338-regulation of transferase activity	17	0.0167412
GO:0048598-embryonic morphogenesis	17	0.0028499
GO:0043549-regulation of kinase activity	15	0.046915
GO:0045892-negative regulation of transcription, DNA-dependent	15	0.0459916
GO:0045859-regulation of protein kinase activity	15	0.0369354
GO:0007167-enzyme linked receptor protein signaling pathway	15	0.0345855
GO:0040008-regulation of growth	15	0.0340059
GO:0051094-positive regulation of developmental process	13	0.0346589
GO:0032535-regulation of cellular component size	13	0.0291296
GO:0060284-regulation of cell development	13	0.0037293
GO:0048729-tissue morphogenesis	13	0.0012635
GO:0045597-positive regulation of cell differentiation	12	0.0213859
GO:0060429-epithelium development	12	0.020185
GO:0001558-regulation of cell growth	12	0.0068033
GO:0051960-regulation of nervous system development	12	0.0063115
GO:0050767-regulation of neurogenesis	12	0.0020893
GO:0007423-sensory organ development	11	0.0476433
GO:0045596-negative regulation of cell differentiation	11	0.0341763
GO:0008361-regulation of cell size	11	0.025893
GO:0045664-regulation of neuron differentiation	10	0.0045224
GO:0051216-cartilage development	10	6.22E-05
GO:0022604-regulation of cell morphogenesis	9	0.0130635
GO:0045165-cell fate commitment	8	0.0484699
GO:0048562-embryonic organ morphogenesis	8	0.0397577
GO:0048705-skeletal system morphogenesis	8	0.0175327
GO:0016051-carbohydrate biosynthetic process	8	0.0139383
GO:0007178-transmembrane receptor protein serine/threonine kinase signaling pathway	8	0.011469
GO:0002009-morphogenesis of an epithelium	8	0.0103611
GO:0007568-aging	7	0.0475366
GO:0001655-urogenital system development	7	0.0475366
GO:0001822-kidney development	7	0.0269717
GO:0009894-regulation of catabolic process	7	0.0269717
GO:0010769-regulation of cell morphogenesis involved in differentiation	7	0.009995
GO:0009612-response to mechanical stimulus	7	0.0020711
GO:0048706-embryonic skeletal system development	6	0.0364141
GO:0010975-regulation of neuron projection development	6	0.0254655
GO:0030509-BMP signaling pathway	6	0.0037585
GO:0048704-embryonic skeletal system morphogenesis	5	0.0464755
GO:0042476-odontogenesis	5	0.0392947
GO:0009064-glutamine family amino acid metabolic process	5	0.0348867
GO:0001656-metanephros development	5	0.0202532
GO:0001709-cell fate determination	5	0.0074804
GO:0030199-collagen fibril organization	5	0.004677
GO:0001657-ureteric bud development	4	0.0499349
GO:0070167-regulation of biomineral formation	4	0.039845
GO:0030500-regulation of bone mineralization	4	0.0337599

Table S4. GO analysis of KDM4B-dependent genes at basal level (Related to Figure 6)

GO Term	Count	P Value
GO:0045449-regulation of transcription	299	0.01623
GO:0006350-transcription	249	0.00816
GO:0008104-protein localization	122	5.00E-04
GO:0006793-phosphorus metabolic process	120	0.02376
GO:0006796-phosphate metabolic process	120	0.02376
GO:0045184-establishment of protein localization	107	9.40E-04
GO:0015031-protein transport	105	0.00145
GO:0010941-regulation of cell death	103	0.01962
GO:0043067-regulation of programmed cell death	102	0.02338
GO:0042981-regulation of apoptosis	101	0.02355
GO:0016265-death	97	0.00515
GO:0008219-cell death	97	0.00424
GO:0043933-macromolecular complex subunit organization	91	0.02036
GO:0006357-regulation of transcription from RNA polymerase II promoter	90	0.04473
GO:0065003-macromolecular complex assembly	90	0.00526
GO:0022610-biological adhesion	87	0.04578
GO:0006468-protein amino acid phosphorylation	85	0.02819
GO:0012501-programmed cell death	85	0.00331
GO:0006915-apoptosis	85	0.00219
GO:0006461-protein complex assembly	76	6.66E-04
GO:0070271-protein complex biogenesis	76	6.66E-04
GO:0006396-RNA processing	71	0.03116
GO:0007010-cytoskeleton organization	71	1.01E-04
GO:0010942-positive regulation of cell death	61	0.0111
GO:0043068-positive regulation of programmed cell death	60	0.01478
GO:0043065-positive regulation of apoptosis	60	0.01278
GO:0070272-cellular macromolecule localization	58	0.01345
GO:0034613-cellular protein localization	57	0.01722
GO:0006886-intracellular protein transport	50	0.04484
GO:0060548-negative regulation of cell death	50	0.02508
GO:0043069-negative regulation of programmed cell death	50	0.02386
GO:0008285-negative regulation of cell proliferation	49	0.03766
GO:0043066-negative regulation of apoptosis	49	0.02702
GO:0001501-skeletal system development	49	0.00449
GO:0007167-enzyme linked receptor protein signaling pathway	48	0.02374
GO:0012502-induction of programmed cell death	47	0.0127
GO:0006917-induction of apoptosis	47	0.01199
GO:0030029-actin filament-based process	42	8.48E-04
GO:0030036-actin cytoskeleton organization	41	4.36E-04
GO:0034660-ncRNA metabolic process	37	0.00694
GO:0043062-extracellular structure organization	37	7.20E-06
GO:0001944-vasculature development	36	0.03867
GO:0007517-muscle organ development	36	0.00302
GO:0001568-blood vessel development	35	0.04353
GO:0030097-hemopoiesis	34	0.04222
GO:0048514-blood vessel morphogenesis	33	0.01621
GO:0010608-posttranscriptional regulation of gene expression	32	0.0266
GO:0030198-extracellular matrix organization	32	2.81E-08
GO:0008202-steroid metabolic process	30	0.04058
GO:0022604-regulation of cell morphogenesis	29	1.32E-04
GO:0043623-cellular protein complex assembly	27	0.01454
GO:0016053-organic acid biosynthetic process	26	0.01541
GO:0046394-carboxylic acid biosynthetic process	26	0.01541
GO:0031589-cell-substrate adhesion	26	1.34E-05
GO:0051169-nuclear transport	25	0.0333
GO:0006913-nucleocytoplasmic transport	25	0.02914
GO:0016311-dephosphorylation	24	0.04323
GO:0006399-tRNA metabolic process	24	0.0019
GO:0007160-cell-matrix adhesion	24	2.34E-05
GO:0030155-regulation of cell adhesion	23	0.02308
GO:0051493-regulation of cytoskeleton organization	22	0.03801
GO:0032446-protein modification by small protein conjugation	22	0.02851
GO:0016567-protein ubiquitination	21	0.01872
GO:0007018-microtubule-based movement	20	0.02145
GO:0001503-ossification	19	0.04634
GO:0007178-transmembrane receptor protein serine/threonine kinase signaling pathway	19	0.01719
GO:0016125-sterol metabolic process	19	0.01421
GO:0034330-cell junction organization	18	3.74E-05
GO:0051348-negative regulation of transferase activity	17	0.03537
GO:0008203-cholesterol metabolic process	17	0.02477
GO:0033673-negative regulation of kinase activity	17	0.02047
GO:0006469-negative regulation of protein kinase activity	17	0.01511
GO:0006352-transcription initiation	16	0.02119
GO:0008360-regulation of cell shape	16	2.55E-04
GO:0042063-gliogenesis	15	0.0056
GO:0007015-actin filament organization	14	0.03077
GO:0008652-cellular amino acid biosynthetic process	14	0.00156
GO:0034329-cell junction assembly	14	1.53E-04
GO:0051271-negative regulation of cell motion	13	0.02541
GO:0045785-positive regulation of cell adhesion	13	0.01772
GO:0043038-amino acid activation	13	0.00188
GO:0043039-tRNA aminoacylation	13	0.00188
GO:0040013-negative regulation of locomotion	12	0.04503
GO:0051168-nuclear export	12	0.04053
GO:0030336-negative regulation of cell migration	12	0.02891
GO:0045444-fat cell differentiation	12	0.01741
GO:0010001-glial cell differentiation	12	0.01741
GO:0043244-regulation of protein complex disassembly	12	0.01314
GO:0051258-protein polymerization	12	0.00972
GO:0010810-regulation of cell-substrate adhesion	11	0.01672
GO:0017015-regulation of transforming growth factor beta receptor signaling pathway	11	0.00504
GO:0016126-sterol biosynthetic process	11	0.00213
GO:0043242-negative regulation of protein complex disassembly	10	0.0213
GO:0030199-collagen fibril organization	10	0.00187

Table 5. GO analysis of KDM4B-dependent genes induced by BMP4/7 at 4hr (Related to Figure 6)

GO Term	Count	P Value
GO:0007242-intracellular signaling cascade	52	0.01391
GO:0010604-positive regulation of macromolecule metabolic process	39	0.00904
GO:0042127-regulation of cell proliferation	35	0.01884
GO:0010941-regulation of cell death	34	0.04482
GO:0043933-macromolecular complex subunit organization	32	0.02138
GO:0065003-macromolecular complex assembly	32	0.0091
GO:0010605-negative regulation of macromolecule metabolic process	31	0.04825
GO:0006461-protein complex assembly	27	0.00483
GO:0070271-protein complex biogenesis	27	0.00483
GO:0033554-cellular response to stress	26	0.0328
GO:0001501-skeletal system development	25	3.10E-05
GO:0007010-cytoskeleton organization	23	0.01134
GO:0048598-embryonic morphogenesis	19	0.00498
GO:0060548-negative regulation of cell death	18	0.04231
GO:0043069-negative regulation of programmed cell death	18	0.04148
GO:0043066-negative regulation of apoptosis	18	0.03676
GO:0044271-nitrogen compound biosynthetic process	18	0.01795
GO:0040008-regulation of growth	17	0.04978
GO:0051247-positive regulation of protein metabolic process	15	0.01431
GO:0032990-cell part morphogenesis	14	0.04354
GO:0030029-actin filament-based process	14	0.02885
GO:0032270-positive regulation of cellular protein metabolic process	14	0.02266
GO:0030036-actin cytoskeleton organization	14	0.01818
GO:0045596-negative regulation of cell differentiation	14	0.0129
GO:0006366-transcription from RNA polymerase II promoter	13	0.04738
GO:0045597-positive regulation of cell differentiation	13	0.04211
GO:0007423-sensory organ development	13	0.04211
GO:0031401-positive regulation of protein modification process	13	0.01029
GO:0006163-purine nucleotide metabolic process	13	0.00988
GO:0060348-bone development	13	3.03E-04
GO:0001503-ossification	13	1.61E-04
GO:0048705-skeletal system morphogenesis	13	1.25E-04
GO:0048667-cell morphogenesis involved in neuron differentiation	12	0.04876
GO:0007409-axonogenesis	12	0.02991
GO:0032269-negative regulation of cellular protein metabolic process	11	0.04323
GO:0048729-tissue morphogenesis	11	0.04323
GO:0007178-transmembrane receptor protein serine/threonine kinase signaling pathway	11	9.86E-04
GO:0051216-cartilage development	11	6.45E-05
GO:0009259-ribonucleotide metabolic process	10	0.03184
GO:0030198-extracellular matrix organization	10	0.00384
GO:0009260-ribonucleotide biosynthetic process	9	0.03199
GO:0048736-appendage development	9	0.01175
GO:0060173-limb development	9	0.01175
GO:0045937-positive regulation of phosphate metabolic process	8	0.0297
GO:0010562-positive regulation of phosphorus metabolic process	8	0.0297
GO:0035107-appendage morphogenesis	8	0.02831
GO:0035108-limb morphogenesis	8	0.02831
GO:0035113-embryonic appendage morphogenesis	8	0.01499
GO:0030326-embryonic limb morphogenesis	8	0.01499
GO:0001934-positive regulation of protein amino acid phosphorylation	7	0.04958
GO:0009266-response to temperature stimulus	7	0.03725
GO:0030278-regulation of ossification	7	0.02864
GO:0030509-BMP signaling pathway	7	0.00182
GO:0009123-nucleoside monophosphate metabolic process	6	0.04655
GO:0009408-response to heat	6	0.02523
GO:0009612-response to mechanical stimulus	6	0.02523
GO:0051291-protein heterooligomerization	6	0.01889
GO:0045667-regulation of osteoblast differentiation	6	0.00869
GO:0001649-osteoblast differentiation	6	0.00787
GO:0030199-collagen fibril organization	6	0.00151
GO:0060349-bone morphogenesis	6	2.45E-04
GO:0060350-endochondral bone morphogenesis	6	7.62E-05
GO:0001958-endochondral ossification	6	1.52E-05
GO:0017015-regulation of transforming growth factor beta receptor signaling pathway	5	0.02808
GO:0048332-mesoderm morphogenesis	5	0.02579
GO:0045669-positive regulation of osteoblast differentiation	5	0.00598
GO:0002062-chondrocyte differentiation	5	0.0017
GO:0014013-regulation of gliogenesis	4	0.02343
GO:0001502-cartilage condensation	4	0.01784
GO:0002063-chondrocyte development	4	8.40E-04
GO:0033158-regulation of protein import into nucleus, translocation	3	0.02774
GO:0033160-positive regulation of protein import into nucleus, translocation	3	0.01683
GO:0060391-positive regulation of SMAD protein nuclear translocation	3	0.01226
GO:0060390-regulation of SMAD protein nuclear translocation	3	0.01226
GO:0060395-SMAD protein signal transduction	3	0.01226

Table S6. GO analysis of KDM4B-dependent genes induced by BMP4/7 at 24hr (Related to Figure 6)

GO Term	Count	P Value
GO:0006793-phosphorus metabolic process	34	0.0111238
GO:0006796-phosphate metabolic process	34	0.0111238
GO:0016310-phosphorylation	30	0.00713318
GO:0006468-protein amino acid phosphorylation	25	0.01488107
GO:0043933-macromolecular complex subunit organization	24	0.04783164
GO:0065003-macromolecular complex assembly	23	0.04325222
GO:0007167-enzyme linked receptor protein signaling pathway	21	9.02E-05
GO:0070271-protein complex biogenesis	20	0.01925059
GO:0006461-protein complex assembly	20	0.01925059
GO:0019220-regulation of phosphate metabolic process	18	0.04592089
GO:0051174-regulation of phosphorus metabolic process	18	0.04592089
GO:0042325-regulation of phosphorylation	18	0.03349345
GO:0001501-skeletal system development	18	8.58E-04
GO:0040008-regulation of growth	15	0.02172564
GO:0048598-embryonic morphogenesis	15	0.00945491
GO:0009792-embryonic development ending in birth or egg hatching	14	0.03813864
GO:0043009-chordate embryonic development	14	0.03620641
GO:0048729-tissue morphogenesis	13	7.54E-04
GO:0051347-positive regulation of transferase activity	11	0.04427034
GO:0033674-positive regulation of kinase activity	11	0.03577569
GO:0007169-transmembrane receptor protein tyrosine kinase signaling pathway	11	0.0298722
GO:0035295-tube development	11	0.02686151
GO:0010035-response to inorganic substance	10	0.04172587
GO:0040007-growth	10	0.02234904
GO:0048705-skeletal system morphogenesis	10	9.20E-04
GO:0051259-protein oligomerization	9	0.04224654
GO:0043062-extracellular structure organization	9	0.03045153
GO:0007178-transmembrane receptor protein serine/threonine kinase signaling pathway	9	0.00217885
GO:0051216-cartilage development	9	2.41E-04
GO:0048562-embryonic organ morphogenesis	8	0.03006825
GO:0030198-extracellular matrix organization	8	0.00882001
GO:0048706-embryonic skeletal system development	8	0.00166144
GO:0060173-limb development	7	0.02817143
GO:0048736-appendage development	7	0.02817143
GO:0051260-protein homooligomerization	7	0.01981872
GO:0048704-embryonic skeletal system morphogenesis	7	0.00167013
GO:0030509-BMP signaling pathway	7	4.14E-04
GO:0045017-glycerolipid biosynthetic process	6	0.03357918
GO:0016049-cell growth	5	0.04759007
GO:0010721-negative regulation of cell development	5	0.02217749
GO:0050768-negative regulation of neurogenesis	5	0.01788517
GO:0001656-metanephros development	5	0.01657981
GO:0030199-collagen fibril organization	5	0.00376701
GO:0001657-ureteric bud development	4	0.04297751
GO:0001709-cell fate determination	4	0.03700567

Supplemental Materials and Methods

The primers for histone demethylase profiling are as follows:

GENES	FORWARD	REVERSE
KDM4A	CCTCACTGCGCTGTCTGTAT	CCAGTCGAAGTGAAGCACAT
KDM4B	CGGGTTCTATCTTGTTCACCCG	AAGGAAGCCTCTGGAACACCTG
KDM4C	GGCATAGGTGACAGGGTGTGTC	CGGGGACCAAACCTCTGAAACCCG
KDM4D	CGGGATCTGCACAGATTATCCACCG	AGTTTCTGAGGAGGGCGACCA
KDM5A	GTTTCTTAAGGTGGCAAGTC	TCTTTGTACTGTTCCCTAC
KDM5B	AGCTTTCTCAGAATGTTGGC	GCAGAGTCTGGGAATTACA
KDM5C	GGGTTTCTAAAGTAGATCT	CCACACATCTGAGCTTAGT
KDM5D	ATCTCCTCACCTCTCCAAAG	TTGTCCTAGGCGTGGCCGT
KDM3A	ACCTGCAGTTATTCTTCAGC	TAATGCCAGTCCTATGCCAT
KDM3B	TGTTCCCTGGGGACTCCTCT	GGGCACTACAGTACAGCTGG
JMJD1C	TTTGTGAAGCTATTGACTG	CACTTAACAAAAGCAAGCC
KDM2B	GTTAGTGGTAGTGGTGTGG	AGCAGATGTGGTGTGGTC
KDM2A	CGGATAGTTGAGAAAGCCAAGATCCG	CTCTTGTTGGGCCTCTGTAGC
KDM6A	CGTCCGAGTGTCAACCAACTGGACG	TGAGAGTCCTGGAGTAGGAGCAG
KDM6B	CTCAACTGGGCCTCTTCTC	GCCTGTCAGATCCCAGTTCT
UTY	ATTCTGAAGCAATATCAGAC	TACAGTAATGAGCTGGTTCA
PHF2	TCGGCACTCTCTGTTCTCCC	AAATCCAGCCCCCTCCGTGTC
PTH8	CTTTCTCTACCTTGGGGACC	TAGGGACTCACGTGCTAGGG
KIAA1718	ATCTGTGAACCTTGGAGAGG	TAGGGACTCACGTGCTAGGG
LOC339123	AGCAAGCGACACACACTCAC	GCACCAACTCTTCACAGGA
JMJD4	GGCCCTTCCAGAAATAAAGACC	CAGGCAGTGGCCATGAACAG
JMJD5	GTGGGGAGAGCCCAGAAGGACATT	GACCCACCGTTCCAAAAA
HAIRLESS	AGACCTCTGCCCTCTGCT	GCTTGGAACACAGCCCAGTC
FIH1	TTACTTAACCTCTGAGCC	CCAACAACCCCTGAGGTAGAT
HSPBAP1	ACGTAGAACGCTACACTCGAAG	TAAGCCCAGAACATTGGAATG
JARID2	AAGTGCTGCTTACATCACTG	AGTGGATCATAGGACGTTCC
PTDSR	AGGTGGATCACTTGAGGTCA	CACCACACCTGGCTAATT
PLA2G4B	GCCCAGGCCACACATAATT	AGTGGTAGCTTCATGTGG