

Figure S1. The effect of Prmt1-KO cells.

(A) The mRNA levels of Prmt1 decreased in Prmt1-KO cells. (B) Western blotting with anti-Prmt1, anti-Actin, anti-H4R3me2a, anti-H3R17me, anti-H4, and anti-ASYM25 in E14 ES cells (WT) and Prmt1 KO cells. (C) Western blotting with anti-Prmt1, anti-Actin, and anti-ASYM25 in Fur treated (+) or untreated (-) E14 cells. (D) The disruption of the Prmt1 genomic sequence within the knockout cell lines (KO1 and KO2).

Figure S2

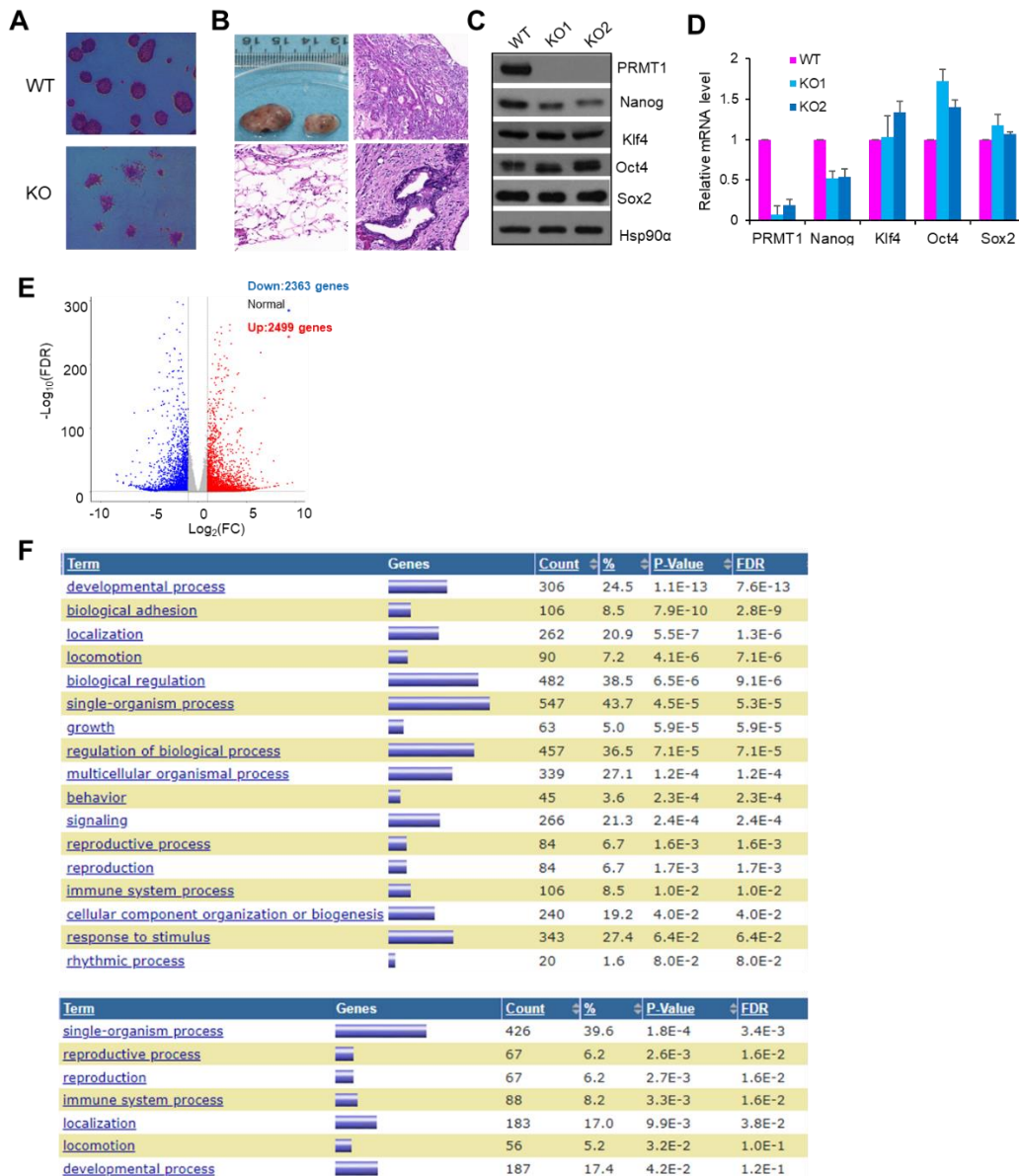


Figure S2. RNA-seq analysis of WT and Prmt1-KO cells.

(A) Alkaline phosphatase staining of WT and Prmt1 KO cells. (B) Hematoxylin and eosin staining of teratoma derived from PRMT1 KO mESCs. (C and D) Expression of the indicated genes by using Western blot (C) and RT-qPCR (D). (E) Differential genes expression analysis of bulk RNA-seq data of WT and Prmt1-KO cells. (F) Enriched GO terms from DAVID 6.8 for Prmt1 upregulated genes (upper panels) and downregulated genes (lower panels) according to the bulk RNA-Seq data of WT and Prmt1 KO cells.

Figure S3

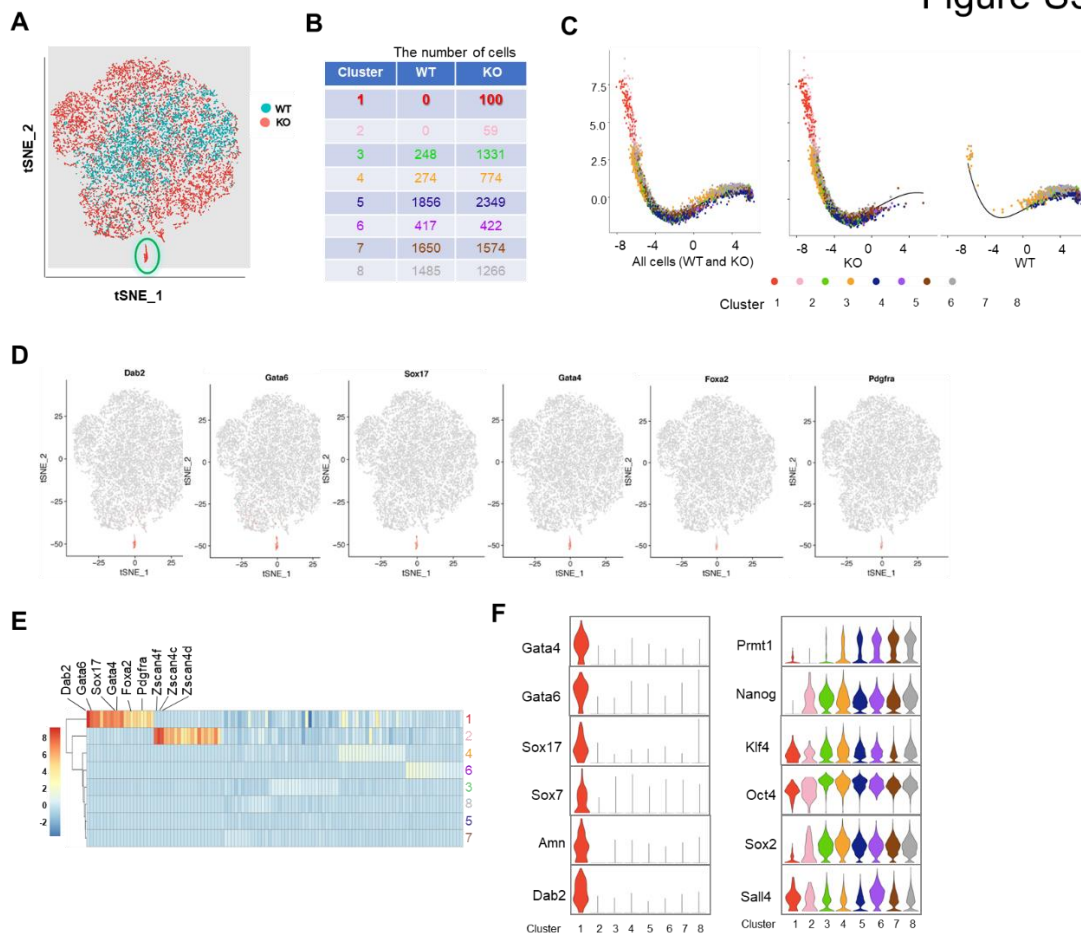


Figure S3. The analysis of sc-RNA seq.

(A) tSNE of 13,805 cells by scRNA-seq, include 5930 WT cells and 7875 Prmt1 KO cells which is related in Figure 4D. (B) Eight transcriptionally distinct clusters were identified (clusters 1-8) by unsupervised classification. Number and origin of cells in each cluster. (C) Principal component analysis (PCA) based on pseudotime showed that cluster 1 was distant from the other clusters. (D) Heatmap displaying the expression of marker genes in each cluster. (E) Cluster 1 and 2 are marked with indicated PrE genes and 2C-like genes. (F) Violin map showed that PrE genes are significantly and specifically high expression in cluster 1.

Figure S4

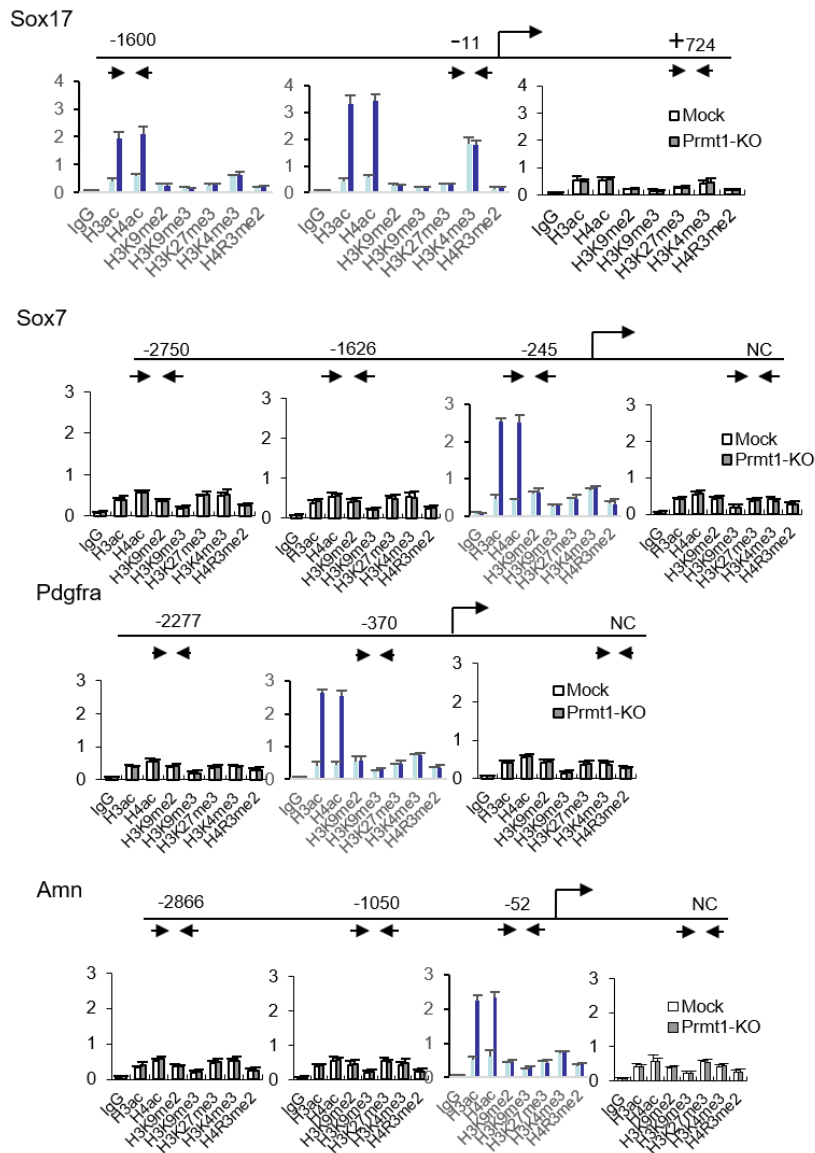


Figure S4. ChIP-qPCR analysis of histone modifications in upstream region of other PrE genes (Sox17, Sox7, Pdgfra, and Amn) in WT and Prmt1-KO cells.

Figure S5

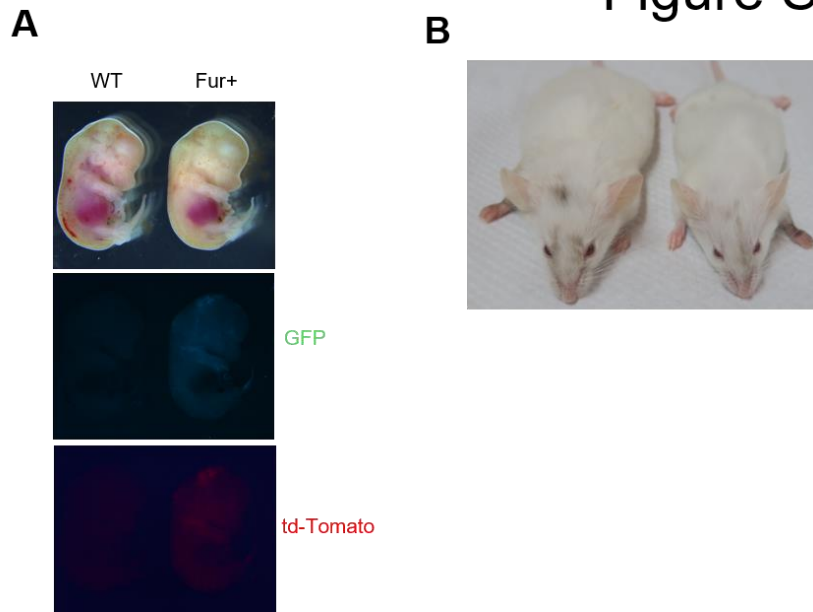


Figure S5. The chimeric embryos at E12.5 (A) and mice after birth (B) showed that the Fur-treated ES cells.

Table S1. The potential off-targeting locus were amplified by PCR and then sequenced, showing no mutant.

off target sequence	loci in genome	forward primer sequence	loci in genome	reverse primer sequence	loci in genome	length	Mutant
TAGTTAGAACCCCAAC ACTGAGG	chr6:+67353 807	CCAACCCTGCTCAACC ATCT	chr6:+67353 436	AGCTTCATTACCCCA GCACC	chr6:+67354 003	567	None
TAGTGAGAAGCCTAAC ACTGAGG	chr18:+4484 501	GTGGCCTTGCAAATCA GCTC	chr18:+4484 239	CCTACTCCACCTTGC CCTTG	chr18:+4484 832	593	None
TAGGGAGAAACCCATC GCTGCAG	chr16:- 72356018	TAAAAACCCATGGCAC TCCC	chr16:- 72356290	CATGTGCCCTTTTCC GTCC	chr16:- 72355895	395	None
CAGTAAGTAGCCCAAC TCTGAGG	chr3:+65369 957	TCCTCCTGTTACCCTC CCTG	chr3:+65369 659	GAACACTCACGGCTT CCTCA	chr3:+65370 340	681	None
GGCTGAGAAGCCCAA CTCTGTAG	chr12:+5140 528	GCTTACTCTGGTCACA ACGC	chr12:+5140 288	AGCAGAAGTGTGCGC TAGG	chr12:+5140 743	455	None
CACTAAGAAGCCCAAC TCTGAGG	chr1:- 5090179	TCAGAACCAAGCAGAG CAGAG	chr1:- 5090364	TGCGCCTCAGAGATG AGTTG	chr1:- 5090019	345	None
TTGACAGAAGCCCAAC CCTGCAG	chr7:- 90034818	TCAGCCACATGAGATG CTGT	chr7:- 90035173	GAATCCAAGGTGTGA TGTGCT	chr7:- 90034415	758	None
TAGTAAGAAGCTCAAC ACTGTAG	chr18:- 42730599	TCACCGCAGAGGTTTC GTC	chr18:- 42730825	CGTGCAGAGTAGTG TCCTATC	chr18:- 42730457	368	None
TAATGAGCACCCCAAC ACTGGGG	chr8:- 118620357	CCCAGGTGAGAGTA GGTGA	chr8:- 118620653	CCTCCAGAGCCTCAC AATCC	chr8:- 118620141	512	None
TAGGCAGAATCCCAAC ACTGAAG	chr13:- 72369346	AGCATGCCTACAACAC TCCC	chr13:- 72369419	GGCACTAGTCCCCT AAGGA	chr13:- 72369067	352	None
CTGGGGGGCTCAAGG TTATTAGG	chr13:- 29104435	GATAACCTGCTGGTAG GGAGC	chr13:- 29104571	CACAACGTGGAGTAG GAGGTC	chr13:- 29104238	333	None
CAGGGGCCACAAGT TTATTGGG	chr1:+18698 616	TCTATGGGTAATGGGC CAGATG	chr1:+18698 447	CACATATAGGGTGGC CCAGT	chr1:+18698 889	442	None
CTGGAGCCCAAGG TTAGTCAG	chr16:+2844 5427	CGGATCAAGGAGCTG GCTAT	chr16:+2844 5244	GGACACCTTACAACG CTTGC	chr16:+2844 5712	468	None
CGGGAGCTCTCAAGG TTAGTCAG	chr11:+7187 9950	TGCCAATCTGCCCCAC TTAG	chr11:+7187 9708	TGAGGAGCTGCAACA AGGAG	chr11:+7188 0138	430	None
AGAGGGCCAGCAAGG TTACTCAG	chr5:- 107733643	ACGGGTAACATAGGG AAAGACAA	chr5:- 107733720	GGGGGCTGCTCATAT CATGG	chr5:- 107733518	202	None
CGGGAGCAAGCAAGG TTCTTGAG	chr6:+14463 2967	AAGGCATGAAAAGTAG AAAAAGCC	chr6:+14463 2835	CGCCTCACACTTCCA TGACA	chr6:+14463 3100	265	None
CAAGGGCCAGCAAGG GTATTGGG	chr4:- 150681700	AACACATCCCACATCC CGAG	chr4:- 150681797	CTTAAGCGGTGCTCT GGGC	chr4:- 150681298	499	None
CGGCCGCCGCAAGC TGATTGAG	chr5:+11917 1445	AGGGCATGAAGTGTA GTGCTC	chr5:+11917 1297	CACGAAAGCCGAAGG GTAGA	chr5:+11917 1807	510	None
CGGGGGCCGAAAAGG TCAGTGAG	chr17:+3602 3172	TTGAGGCTGCCTGTGA GATG	chr17:+3602 3040	TGTCTGCAGCATCCG AAACT	chr17:+3602 3492	452	None
CTGGGGCTGCAAGG CCATTAGG	chr4:- 136242201	GAACGTGTGTGAGGC AGAGA	chr4:- 136242509	CTCCGAGGTTGCAT GAGGT	chr4:- 136241899	610	None
TACAGCATAATCAGAG ATACTGG	chr18:- 4484742	TCCCACCAGTGGATT TGTAGT	chr18:- 4485010	TACACAGCCTCACGT ACTGC	chr18:- 4484573	437	None
AATGGCATAATCGGAG ATACTGG	chr2:+13769 5802	GGAAGTAGCCAGCCC ATTGT	chr2:+13769 5455	TTTTCTGACCCCCAC CACAC	chr2:+13769 6079	624	None
CACACATAATCGTAG ATACAGG	chr13:- 72278554	TCAGGCCCTTAGGCTC TTCT	chr13:- 72278723	GGCCTGCCAGTAGGA TGTTT	chr13:- 72278151	572	None
AGCAGCAAAATGGGA GATACTGG	chr2:- 135266227	AATTGCTGCGCTGTAG ACAT	chr2:- 135266332	GATGAAGCCTCGTTG CCTTT	chr2:- 135265984	348	None
TAAGGCATAATCGGAG ATTCAGG	chr7:- 90200445	AAAGAAAGATGCCCC CAAG	chr7:- 90200372	GGCCAGGCTACATAG CAAAC	chr7:- 90199975	397	None
CATAGCACAAGGGGA GATACAAG	chr1:+75136 224	CCACATCTGCAGAGA AGCA	chr1:+75136 041	GTCCTATTCGCCGAC TCCAG	chr1:+75136 439	398	None
CAGAGCAGAAACGGGA GATAAAAG	chr17:+9441 2138	AACTGCGTGCAATGTG GTGA	chr17:+9441 1914	ATGTACTCGCATGTC CTTGAT	chr17:+9441 2446	532	None
CACAACATACTTGAG ATAGAGG	chr6:- 73676517	GCAGTCTCCATTTTCT CCCTGA	chr6:- 73676729	ACAACCGTTCATAAG GCATCTCT	chr6:- 73676189	540	None
TAGAGCATAATAGGAG ATCCAAG	chrX:+4511 2271	TGACTCTGTTCTCGGC CATT	chrX:+4511 1894	ATGCTCTATTCGTGC CCTTG	chrX:+4511 2279	385	None
TACAGTATAAATGGAG ATACGGG	chr6:+53109 111	CGCAGTGATGAGCA GGCTA	chr6:+53108 863	TTTCTGGACAGGGC AATCC	chr6:+53109 475	612	None
CCTCACCTACTGCAC GCTCAAG	chr1:- 94406823	TGGGAGTGATGGCTT GTGAC	chr1:- 94407114	GCTTTCTCACCCCTA ACCCC	chr1:- 94406601	513	None
CATCACCTTGCTGCAC GCCCAAG	chr2:- 89400838	GGCCTTAGCGGGAAA AATAC	chr2:- 89400958	ATGCTCTCAAGGGG AGTTT	chr2:- 89400577	381	None
GAACACGGTGTGCA CGGCCTGG	chr5:- 115084687	CGGCACATCGTCAACT ACCT	chr5:- 115084758	ATGAGAGGCGAAAGG CCATC	chr5:- 115084525	233	None
CGAGGCCGTGCCGCA CGCTCGGG	chr4:+86503 161	GAACCTTAGGGACCCA AGCC	chr4:+86502 788	AACCGCCTCTCCAT AGTCT	chr4:+86503 394	606	None
CTGCACCATGCGGCA CGCTCCAG	chr2:- 135771092	CAGGCCCTGGTTCTGG AGAG	chr2:- 135771199	TCCTTTTTCCCGTTG CCAT	chr2:- 135770745	454	None
CACCCCTGCTGCAC GCACAGG	chr13:- 96588299	CATCTAGCCACCCCGT TGTT	chr13:- 96588524	TCCCTCTGCTTCCTA GCACT	chr13:- 96588040	484	None

CTACACCCGCTGCAC GCTGCAG	chr1:- 54820537	GCCACCACCTTTGCTA CATCT	chr1:- 54820871	CACTTCAGAGCAGAA GAAAACCC	chr1:- 54820392	479	None
TAAACAGTGCTGCAC TCTCAGG	chr1:+33537 592	AGGCAGGGATCTTGTA GGACT	chr1:+33537 315	ACGTTGTTACCGCT CTGATT	chr1:+33537 827	512	None
CAAGACCCTGGGGCA CGCTCAGG	chr13:+1035 95202	GGCCTGGGTTAGGGT AAACA	chr13:+1035 94932	TGAGTAGAGGCGGTT TCCTC	chr13:+1035 95506	574	None
CATCACGGTCCTGCAC TCTCAAG	chr6:- 3328399	CTGGCTAGGGACTGG TTGTG	chr6:- 3328568	CAGGGGTAGGACAAG GAGGA	chr6:- 3328101	467	None

Table S2. Primers for RT-qPCR and constructions.

Primers for RT-qPCR	
mKlf4-qPCR-F1	GTGCCCGACTAACCGTTG
mKlf4-qPCR-R1	GTCGTTGAACTCCTCGGTCT
mOct4-qPCR-F	ATCACTCACATCGCCAATCA
mOct4-qPCR-R	CCTGGGAAAGGTGTCCTGTA
mSox2-qPCR-F	ATGATGGAGACGGAGCTGAA
mSox2-qPCR-R	TTGCTGATCTCCGAGTTGTG
mNanog-qPCR-F	ACCTGAGCTATAAGCAGGTTAAGAC
mNanog-qPCR-R	GTGCTGAGCCCTTCTGAATCAGAC
mGata4-qPCR-F	CGCCGCCTGTCCGCTTCC
mGata4-qPCR-R	TTGGGCTTCCGTTTTCTGGTTTGA
mGata6-qPCR-F	TGCCTCGACCACTTGCTATGAAAA
mGata6-qPCR-R	CACTGATGCCCTACCCCTGAG
mSox17-qPCR-F	GGAGGGTCACCACTGCTTTA
mSox17-qPCR-R	AGATGTCTGGAGGTGCTGCT
mActb(62-81)-qPCR-F	TCTTTGCAGCTCCTTCGTTG
mActb(193-212)-qPCR-R	ACGATGGAGGGGAATACAGC
Primers for cloning	
mKlf4-F-(EcoRI)	<u>CG GAATTC GCCACC</u> ATGAGGCAGCCA
mKlf4-R-(XhoI)	CCGCTCGAG AAGTGCCTCTTCATGTGTAAGGC
mKlf4-R-(Sall)	<u>ACGCGTCGAC</u> AAAGTGCCTCTTCATGTGTAAGGC
mKlf4-F-(BamHI)	<u>CG GGATCC</u> ATGAGGCAGCCACCTGGCGA
mPrmt1-F	<u>CG GAATTCGCCACC</u> ATGGCGCAGCCGAGGC
mPrmt1-R-(XhoI)	<u>CCGCTCGAG</u> CGCATCCGGTAGTCGGTGG
mPrmt1-R-(Sall)	<u>ACGCGTCGAC</u> CGCATCCGGTAGTCGGTGG
Primers for site mutation	
mKlf4-R387K-F	GAGCCCAAGCCAAAGAAGGGGAAGAAGGTCGTGG
mKlf4-R387K-R	CCACGACCTTCTTCCCTTTTGGCTTGGGCTC
mKlf4-R389K-F	AAGCCAAAGAGGGGAAAAAGGTCGTGGCCCCGG
mKlf4-R389K-R	CCGGGGCCACGACCTTTTTCCCTCTTTGGCTT
mKlf4-R390K-F	CCAAAGAGGGGAAGAAAGTCGTGGCCCCGGAAA
mKlf4-R390K-R	TTCCGGGGCCACGACTTCTTCCCTCTTTGG
mKlf4-R394K-F	AGAAGGTCGTGGCCAAAGAAAAGAACAGCCACC
mKlf4-R394K-R	GGTGGCTGTCTTTTCTTGGGCCACGACCTTCT
mKlf4-R396K-F	TCGTGGCCCCGAAAAAACAGCCACCCACACT
mKlf4-R396K-R	AGTGTGGGTGGCTGTTTTTTCCGGGGCCACGA
mKlf4-R387A-F	GAGCCCAAGCCAAAGGCGGGGAAGAAGGTCGTGG
mKlf4-R387A-R	CCACGACCTTCTTCCCGCTTTGGCTTGGGCTC
mKlf4-R389A-F	AAGCCAAAGAGGGGAGCAAGGTCGTGGCCCCGG
mKlf4-R389A-R	CCGGGGCCACGACCTTGCTCCCTCTTTGGCTT
mKlf4-R390A-F	CCAAAGAGGGGAAGAGCGTCGTGGCCCCGGAAA

mKlf4-R390A-R	TTTCCGGGGCCACGACGCTCTTCCCCTTTTGG
mKlf4-R394A-F	AGAAGGTCGTGGCCCGCGAAAAGAACAGCCACC
mKlf4-R394A-R	GGTGGCTGTTCTTTTCGCGGGCCACGACCTTCT
mKlf4-R396A-F	TCGTGGCCCCGAAAAGCAACAGCCACCCACACT
mKlf4-R396A-R	AGTGTGGGTGGCTGTTGCTTTCCGGGGCCACGA
mKlf4-R394,396A-F	AGAAGGTCGTGGCCC GCGAAA GCAACAGCCACCCACACT
mKlf4-R394,396A-R	AGTGTGGGTGGCTGTTGCTTTTCGCGGGCCACGACCTTCT
mKlf4-R394,396K-F	AGAAGGTCGTGGCCC AAGAAA AAGACAGCCACCCACACT
mKlf4-R394,396K-R	AGTGTGGGTGGCTGTTCTTTTCTTGGGCCACGACCTTCT
mKlf4-R394,396F-F	AGAAGGTCGTGGCCC TCAAAA TTCACAGCCACCCACACT
mKlf4-R394,396F-R	AGTGTGGGTGGCTGTGAATTTGAAGGGCCACGACCTTCT
mKlf4-R387,389K-F	GAGCCCAAGCCAAAGAAGGGAAAAAAGTCGTGGCCCCGG
mKlf4-R387,389K-R	CCGGGGCCAC GACCTTTTTC CCTTCTTTGG CTTGGGCTC
mKlf4-R389,390K-F	AAGCCAAAGAGGGGAAAAAAGTCGTGGCCCCGGAAA
mKlf4-R389,390K-R	TTTCCGGGGC CACGACTTTT TCCCCTCTT TGGCTT
mKlf4-R387,389,390K-F	GAGCCCAAGCCAAAG AAGGGAAAAAAG TCGTGGCCCCGGAAA
mKlf4-R387,389,390K-R	TTTCCGGGGC CACGA CTTT TCCCCTCTT TGGCTTGGGC TC
mKlf4-R387,389,390A-F	GAGCCCAAGCCAAAG GCGGGAGCAGCG TCGTGGCCCCGGAAA
mKlf4-R387,389,390A-R	TTTCCGGGGC CACGA CGCTG CTCCCGCCTT TGGCTTGGGC TC
mKlf4-R387,389,390F-F	GAGCCCAAGCCAAAG TTCGGATTCTC TCGTGGCCCCGGAAA
mKlf4-R387,389,390F-R	TTTCCGGGGC CACGA GAAGAA TCC GAA CTTT GGCTTGGGC TC
mKlf4-R387,389,390,394,396A-F	GCAGCGTCGTGGCCCGCGAAAAGCAACAGCCACCCACACT
mKlf4-R387,389,390,394,396A-R	AGTGTGGGTG GCTGTTGCTT TCGCGGGCCA CGACGCTGC
mKlf4-R387,389,390,394,396K-F	AAAAAGTCGTGGCCCAAGAAAAAACAGCCACCCACACT
mKlf4-R387,389,390,394,396K-R	AGTGTGGGTG GCTGTTTTT TCTTGGGCCA CGACTTTTT
Primers for Klf4 truncations	
mKlf4(1-157)-F	CGCGGATCCATGAGGCAGCCACCTGGCGAG
mKlf4(1-157)-R	CCGCTCGAGTTACGGGTCACCCCGGCCCGGAT
mKlf4(1-184)-F	CGCGGATCCATGAGGCAGCCACCTGGCGAG
mKlf4(1-184)-R	CCGCTCGAGCAGGTTGAAGGGGGCCGTG
mKlf4(1-400)-F	CGCGGATCCATGAGGCAGCCACCTGGCGAG
mKlf4(1-400)-R	CCGCTCGAGTTAGTGGGTGGCTGTTCTTTT
mKlf4(1-425)-F	CGCGGATCCATGAGGCAGCCACCTGGCGAG
mKlf4(1-425)-R	CCGCTCGAGTTATGTGTGAGTTCGCAGGTG
mKlf4(158-385)-F	CGCGGATCCGCGTGGCTGCCAGCAACACA
mKlf4(158-385)-R	CCGCTCGAGTTATGGCTTGGGCTCCTCTGGCAG
mKlf4(463-483)-F	CGCGGATCCGACCTGGCGGCGACGGTGGCC
mKlf4(463-483)-R	CCGCTCGAGTAAAAGTGCCTCTTCATGTG
mKlf4(117-483)-F	CGCGGATCCGTGGCCGCCACCGTGACCACC
mKlf4(117-483)-R	CCGCTCGAGTAAAAGTGCCTCTTCATGTG
mKlf4(158-483)-F	CGCGGATCCGCGTGGCTGCCAGCAACACA
mKlf4(158-483)-R	CCGCTCGAGTAAAAGTGCCTCTTCATGTG
mKlf4(185-483)-F	CGCGGATCCGCGGACATCAATGACGTGAGC

mKlf4(185-483)-R	CCGCTCGAGTAAAAAGTGCCTCTTCATGTG
mKlf4(386-483)-F	CGCGGATCCAAGAGGGGAAGAAGGTCTGTGG
mKlf4(386-483)-R	CCGCTCGAGTAAAAAGTGCCTCTTCATGTG

Table S3. Primers for CHIP qPCR assay

	Sequence (5'-3')
Gata4 (-541/-337)-F	CGGCTCGTGGGAAGGAGAA
Gata4 (-541/-337)-R	CGGCTCGTGGGAAGGAGAA
Gata4 (+8050/+8187)-F	TCGGAGAAGAGTGAGCAG
Gata4 (+8050/+8187)-R	GTGACAGCCATAGCCAAA
Gata6 (-556/-349)-F	TCTCCGAGTTATCACAGCG
Gata6 (-556/-349)-R	GAGCAGGAAGAATGACAGG
Gata6 (+675/+820)-F	CCCATCTCGTCTTCGTCC
Gata6 (+675/+820)-R	TGCGAGGCGTAGGGGCTGA
Sox17 v1 (-219/-4)-F	CAGTTTACTTCTGCTTCG
Sox17 v1 ((-219/-4)-R	GCTGAGAACGTCTGACCC
Sox17 v1 (+2976/+3104)-F	AGGCTAACAGTCTTACACGC
Sox17 v1 (+2976/+3104)-R	TTCCATCGCAAACACCAC
Sox17 v2 (-36/+179)-F	GGCAGGTGTAGCCAGAAC
Sox17 v2 (-36/+179)-R	CCTAACCTTCGCCTAAT
Sox17 v2 (+724/+906)-F	ACTCAATCCCTTCTTCCAGC
Sox17 v2 (+724/+906)-R	CCTCCCTTACCTTTCTCCC
Sox7 (-245/-58)-F	ACCTGCACCGGAGCGGGATC
Sox7 (-245/-58)-R	TATCAGCTTCGGGCCACC
Sox7 (+2796/+3029)-F	ATGCCTCGTCTCTTCAC
Sox7 (+2796/+3029)-R	TCTATTCACCATACCCTACCA
Pdgfra (-440/-273)-F	GTCCAGACAGGTGATCGGTGGTGC
Pdgfra (-440/-273)-R	GGGGCTGGGCTTCTTCCTGGT
Pdgfra (+1216/+1319)-F	AAAGTGTTGAGGCTGCTGTGA
Pdgfra (+1216/+1319)-R	GCCCGAAGAGTTTCTGGTTTA
Amn (-1147 -892)-F	CAACCCACCAACCAAAC
Amn (-1147 -892)-R	GGAAACAGACAGTAGATGAGGC
Amn (-157/+97)-F	AGGGCAGATGCTAAAGCC
Amn (-157/+97)-R	CAGCCTCAATCAAGGTCCAG
Amn (+560 /+745)-F	GGCGACACTCAGCCTTCCT
Amn (+560 /+745)-R	CCCACCTCCAGTTCATCCC