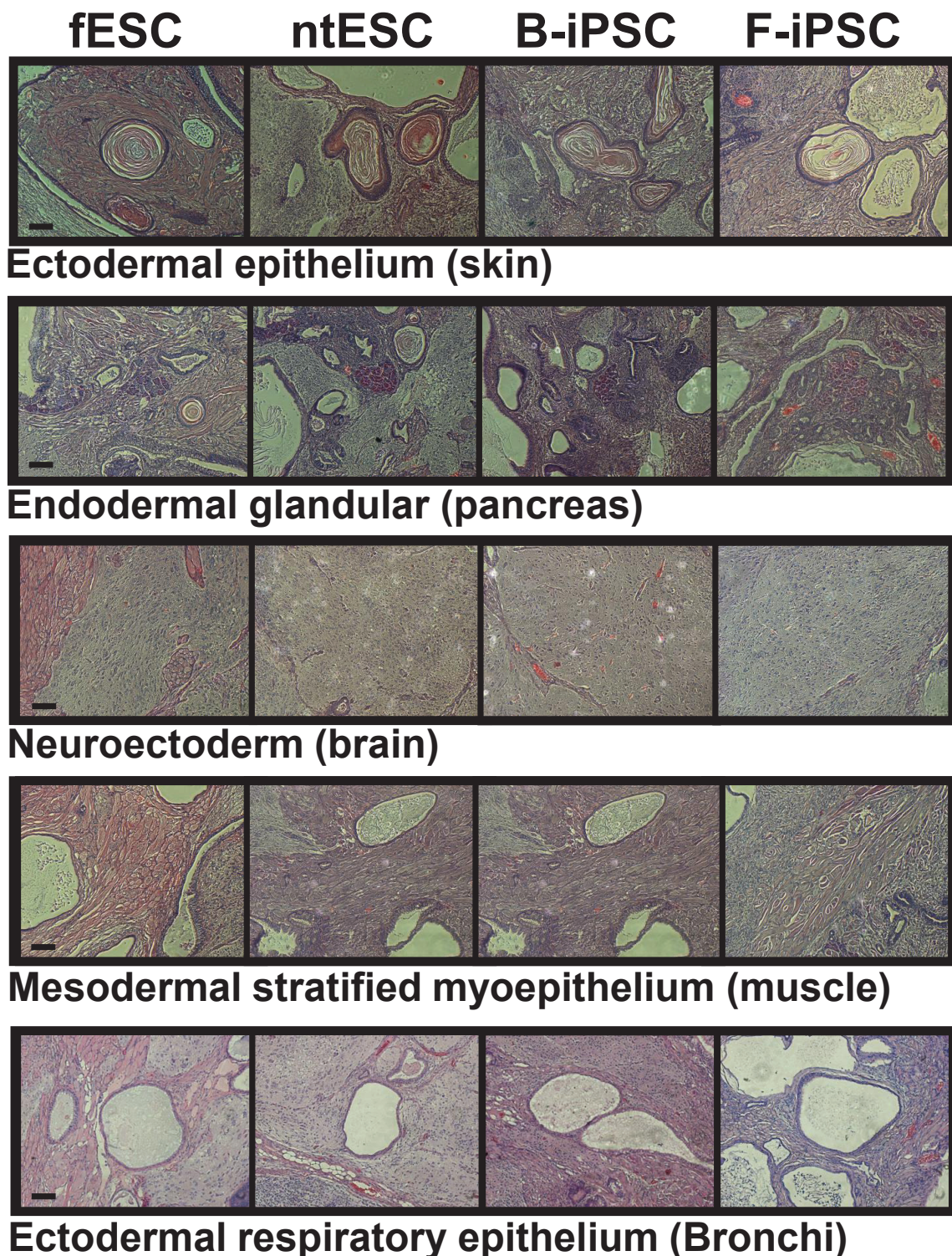
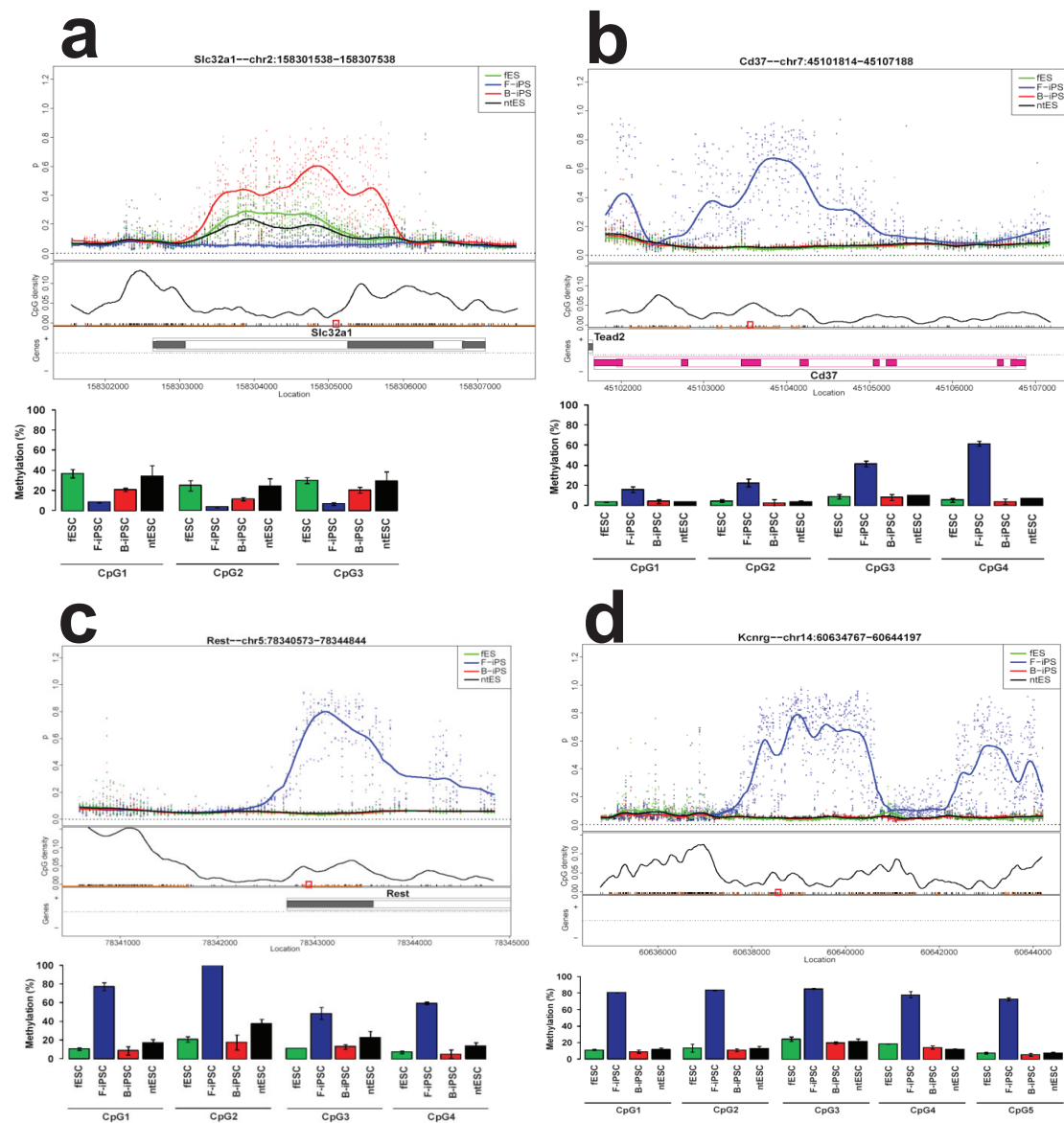


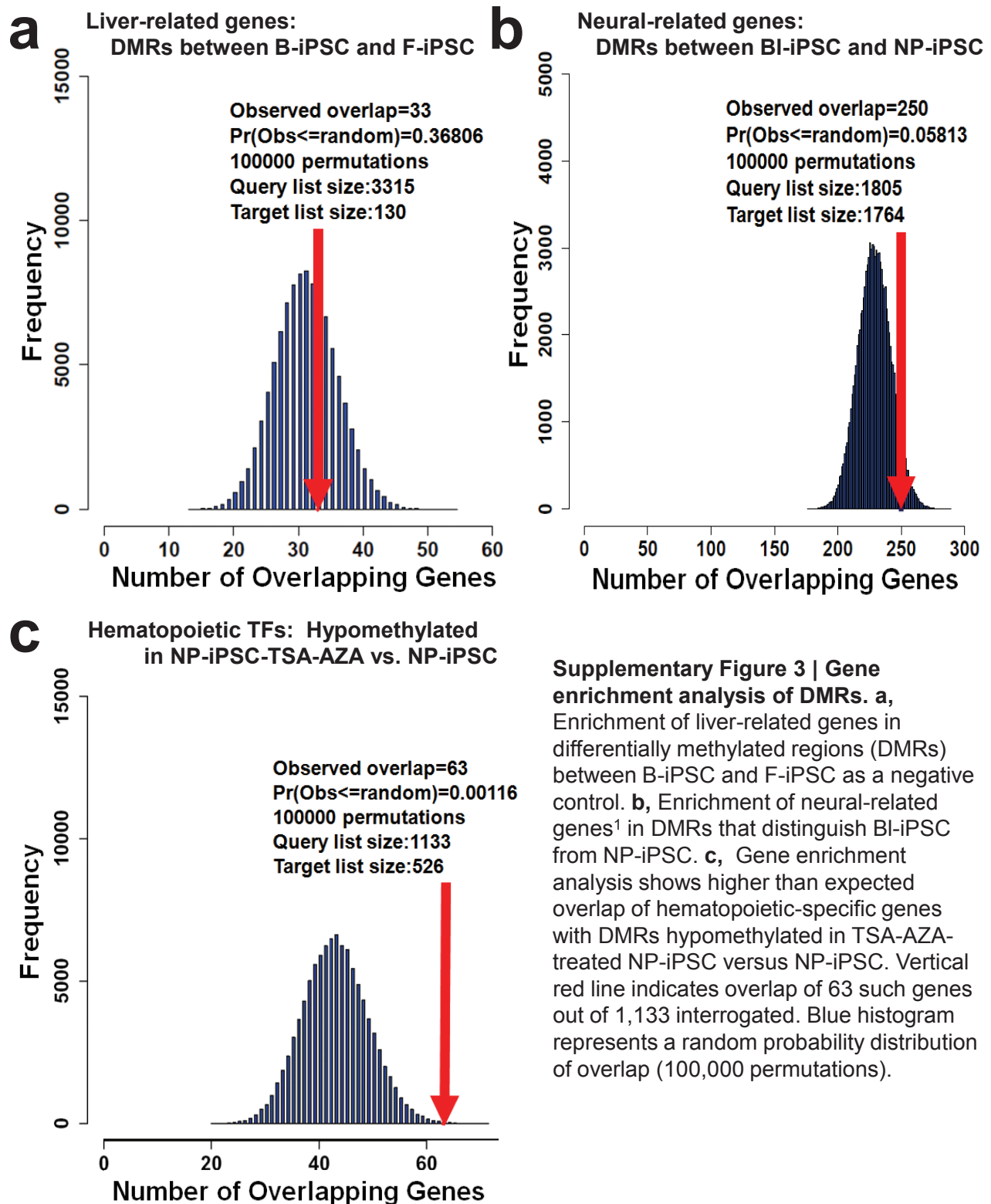
## SUPPLEMENTARY INFORMATION



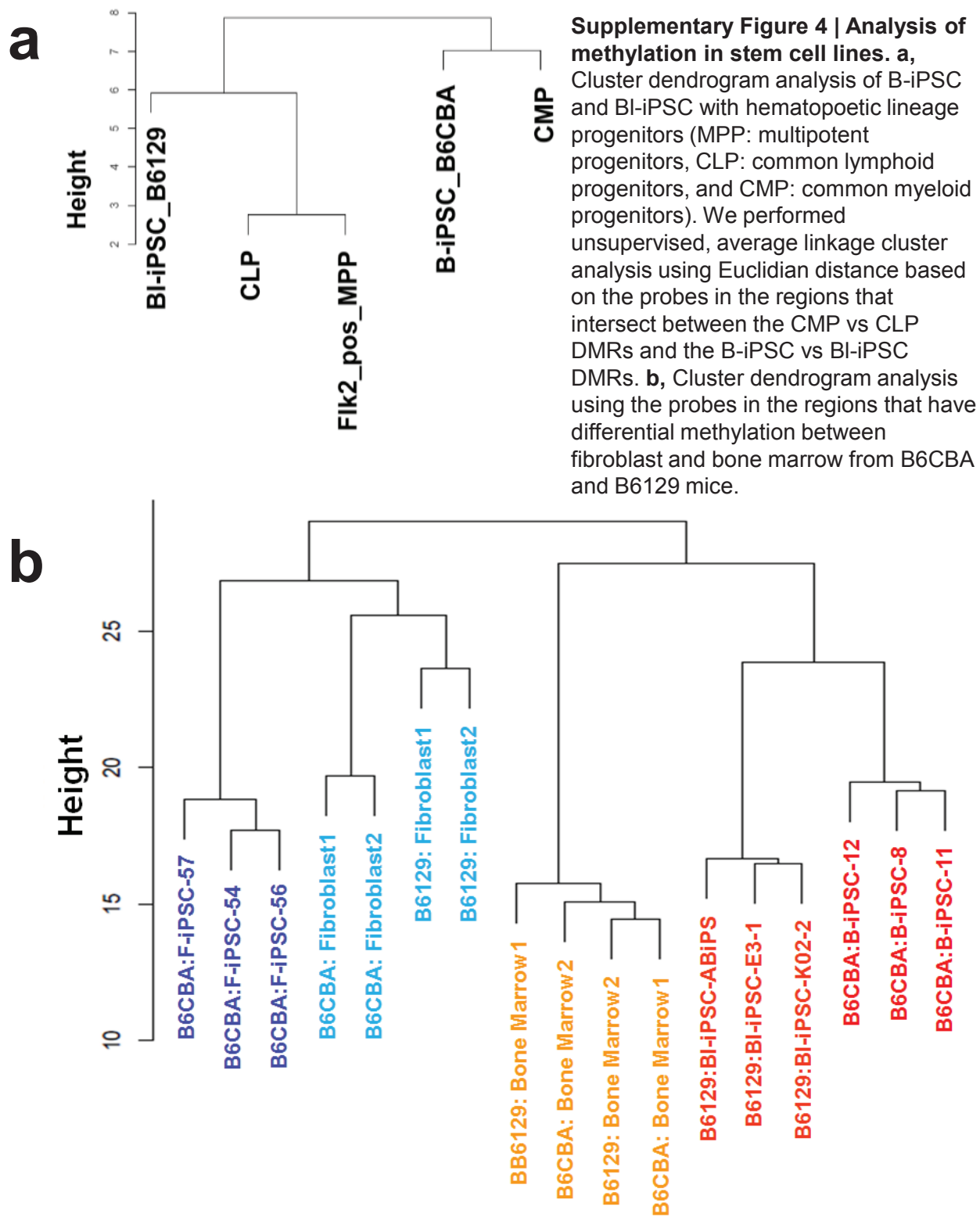
**Supplementary Figure 1 | Teratoma analysis of the fESC, ntESC, B-iPSC, and F-iPSC.** Ectodermal epithelium (skin), Endodermal glandular (pancreas), Neuroectoderm (brain), Mesodermal stratified myoepithelium (muscle), and Ectodermal respiratory epithelium (Bronchi). Scale bar, 500 $\mu$ m.



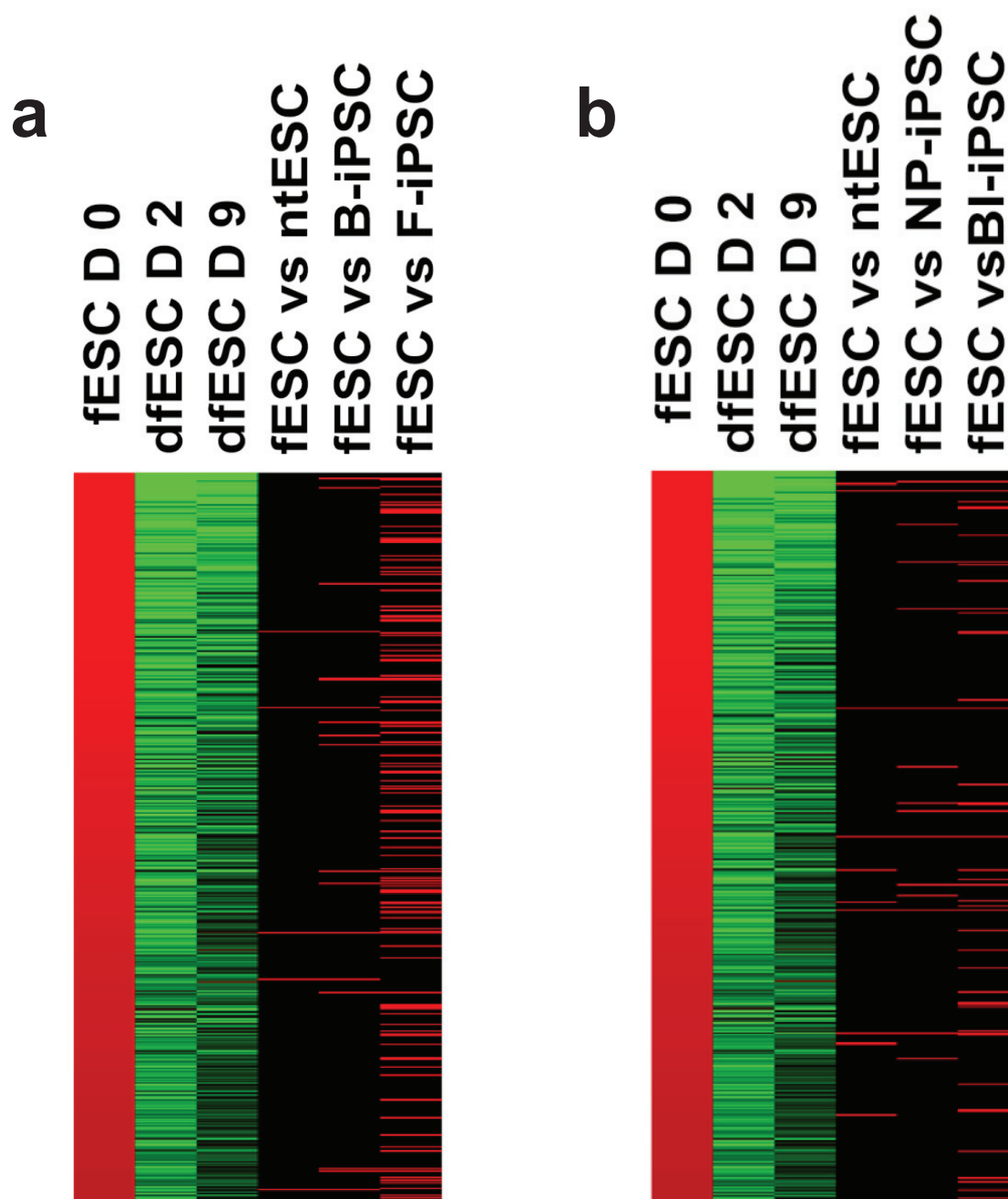
**Supplementary Figure 2 | Examples of differential DNA methylation (upper panels) and confirmation by bisulfite pyrosequencing (lower panels).** The upper panel is a plot of p (percent methylation) value versus genomic location, where the curve represents averaged smoothed p values. The location of CpG dinucleotide (black tick marks on x axis), CpG density (smoothed black line) calculated across the region using a standard density estimator, location of CpG islands (orange line), as well as gene annotation indicating the transcript (thin outer gray line), coding region (thin inner gray line), exons (filled gray box) and gene transcription directionality on the y axis (sense marked as +, antisense as -) are also shown in the upper panels. The lower panel represents the degree of DNA methylation as measured by bisulfite pyrosequencing. The red box indicated on the x axis of the CpG density plot in the upper panels indicates the CpG sites that were measured. Examples are shown for **a**, *Slc32a1*, **b**, *Cd37*, **c**, *Rest*, and **d**, *Kcnrg*.



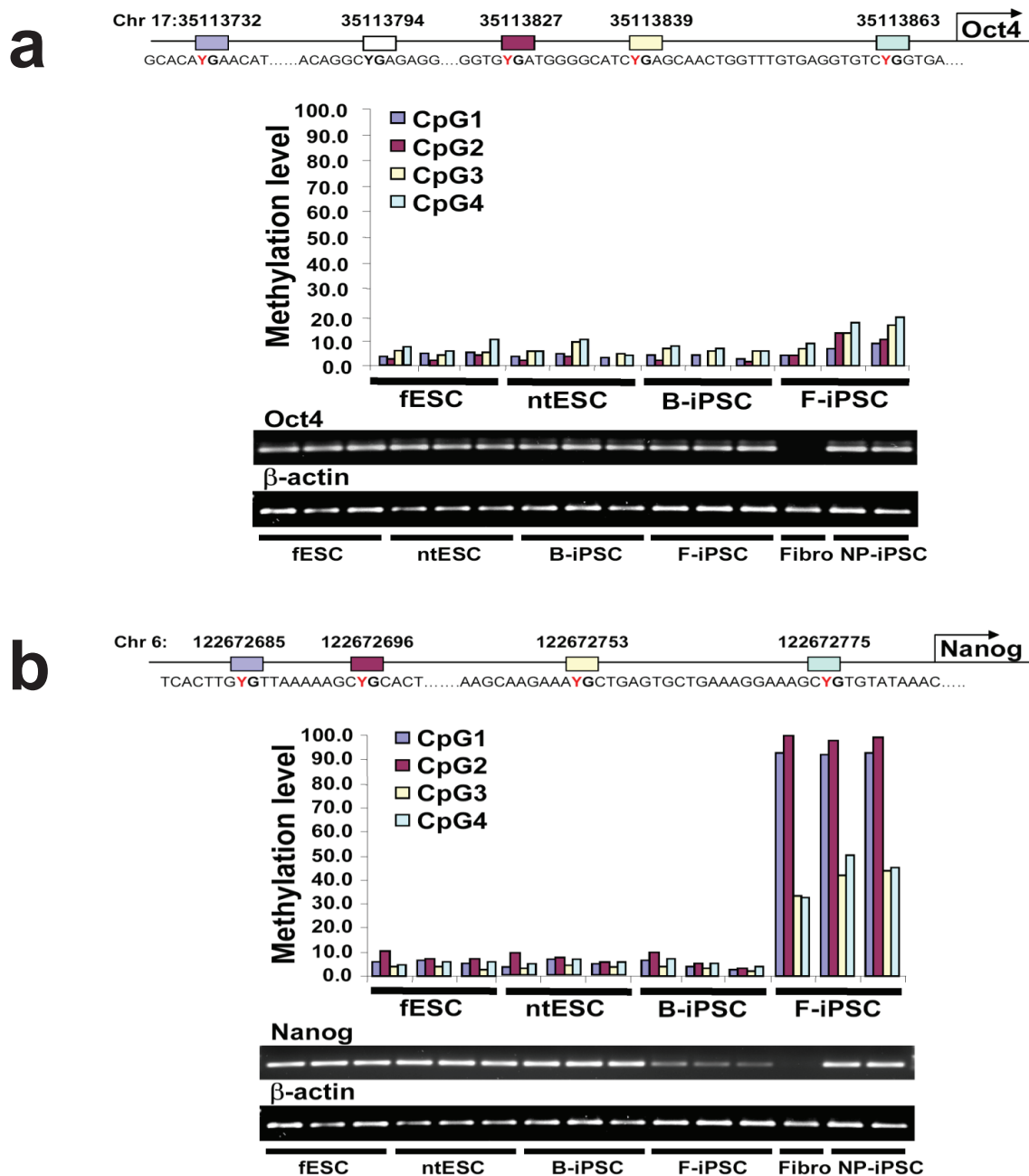




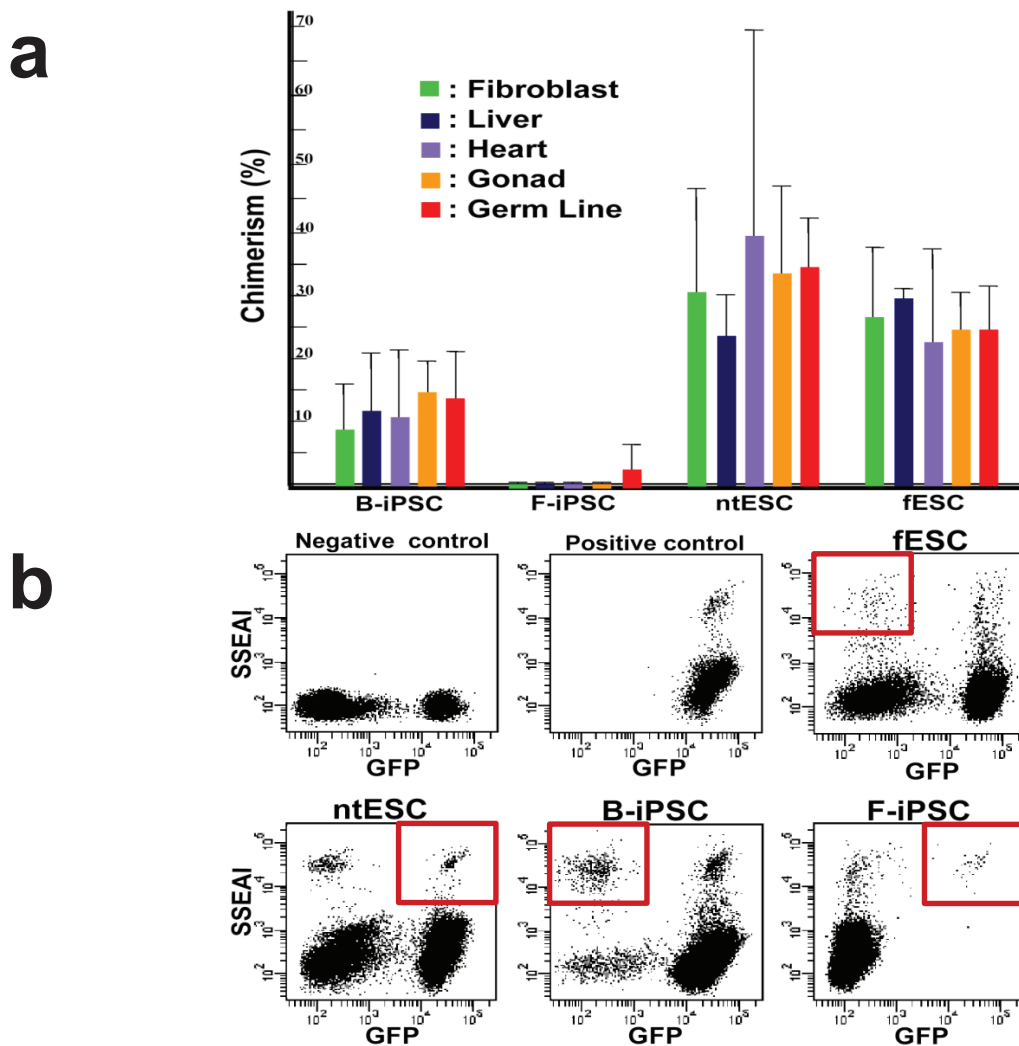




**Supplementary Figure 5 | Overlap of DMRs with loci of genes showing fESC-specific gene expression** (determined from compiled microarray data<sup>2</sup>). Heat maps reflect expression values of fESC-specific genes in undifferentiated state (fESC D0; top 5% highly expressed genes; 554 genes) and after differentiation for 2 and 9 days (differentiated fESC day 2; dfESC D2 and day 9; dfESC D9). **a**, Red bars in the right three lanes indicate number of fESC-specific genes that overlap with DMRs (ntESC, n=5; B-iPSC, n=18; F-iPSC, n=114). **b**, Red bars in the right three lanes indicate number of fESC-specific genes that overlap with DMRs (ntESC, n=12; NP-iPSC, n=16; BI-iPSC, n=45).

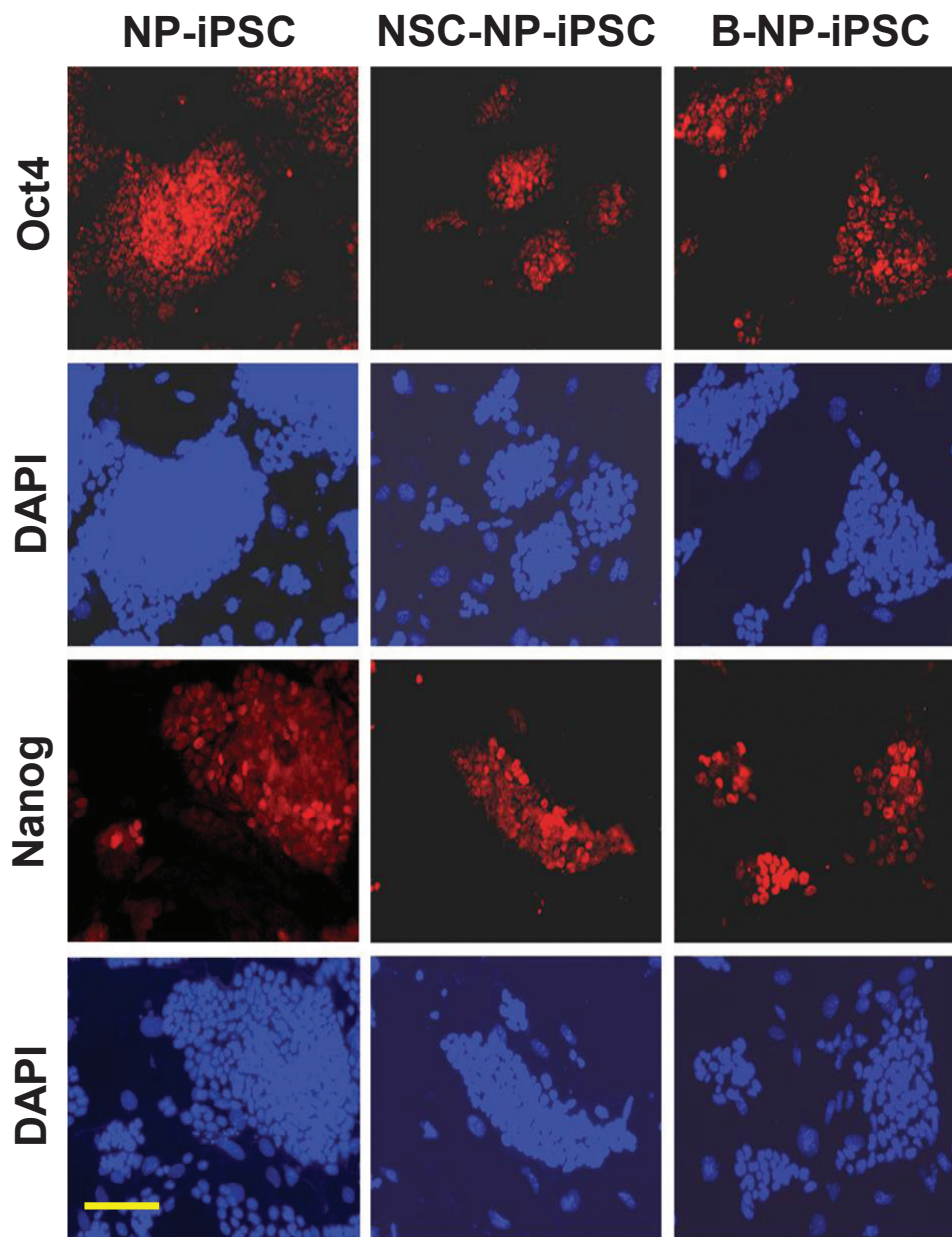


**Supplementary Figure 6 | DNA demethylation of promoters and gene expression on the selected pluripotent gene loci. a, Oct4 b, Nanog.** Schematic structure of the promoters are shown on top, and methylation status of the CpG sites measured by bisulfite pyrosequencing with three independent samples of fESC, ntESC, B-iPSC, and F-iPSC are shown in middle graphs. Detection of Oct4 and Nanog gene expression by RT-PCR with three independent samples of fESC, ntESC, B-iPSC, and F-iPSC are shown below each panel.

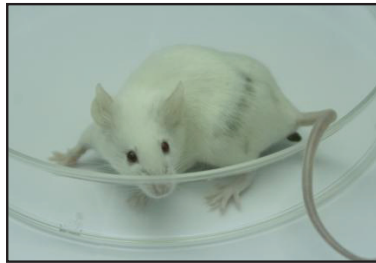


**Supplementary Figure 7 | Chimera analysis of the fESC, ntESC, B-iPSC, and F-iPSC (refer to Fig. 1a).** **a**, Organ chimerism. B6CBA-derived cells were injected into blastocysts and transferred to pseudopregnant mice (N=3 clones of each stem cell type). Organs from E12.5 embryo (B-iPSC, n=14; F-iPSC, n=8; ntESC, n=15; fESC, n=13) were analyzed by flow cytometry to determine % GFP+ cells. Fibroblasts (MEF) were cultured *in vitro* for a week before analysis. The F-iPSC show poor contribution to not only fibroblasts but also to the entire spectrum of tissues, thus suggesting poor incorporation into the blastocyst. *In vivo* chimerism does not obviously reflect lineage bias, but also represents a very different assay from the *in vitro* analysis that is the focus of the paper. Error bars = s.d. **b**, Germline transmission by flow cytometry analysis. Germ cells are represented by SSEA1+ cells of the embryonic gonad. fESC and B-iPSC don't contain GFP markers, but ntESC and F-iPSC harbor GFP markers. Donor cells were discriminated by GFP+ marker from either donor cells or blastocyst. SSEA1+ cells from donor cells were indicated in the red box in the panels. Negative control: SSEA1 staining of heart cells from ntESC chimera mouse; Positive control: SSEA1 staining of gonad cells from GFP+ transgenic mouse.

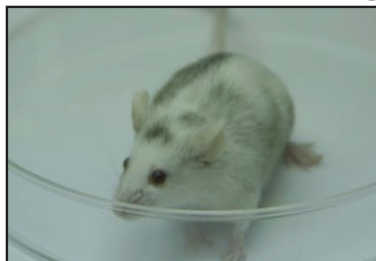




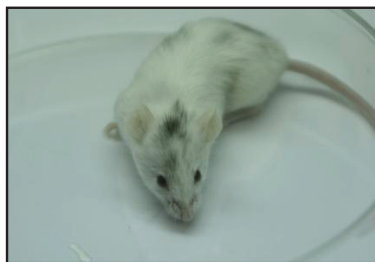
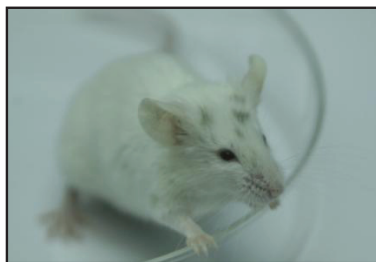
**Supplementary Figure 8 | Immunohistochemistry of NP-iPSC, NSC-NP-iPSC, and B-NP-iPSC for OCT4 and NANOG expression, as indicated.** 4,6-Diamidino-2-phenylindole (DAPI) staining for total cell content. Fibroblasts surrounding pluripotent colonies serve as negative controls for immunohistochemistry staining. Scale bar, 200 $\mu$ m.



**fESC Chimera and germ line transmission**

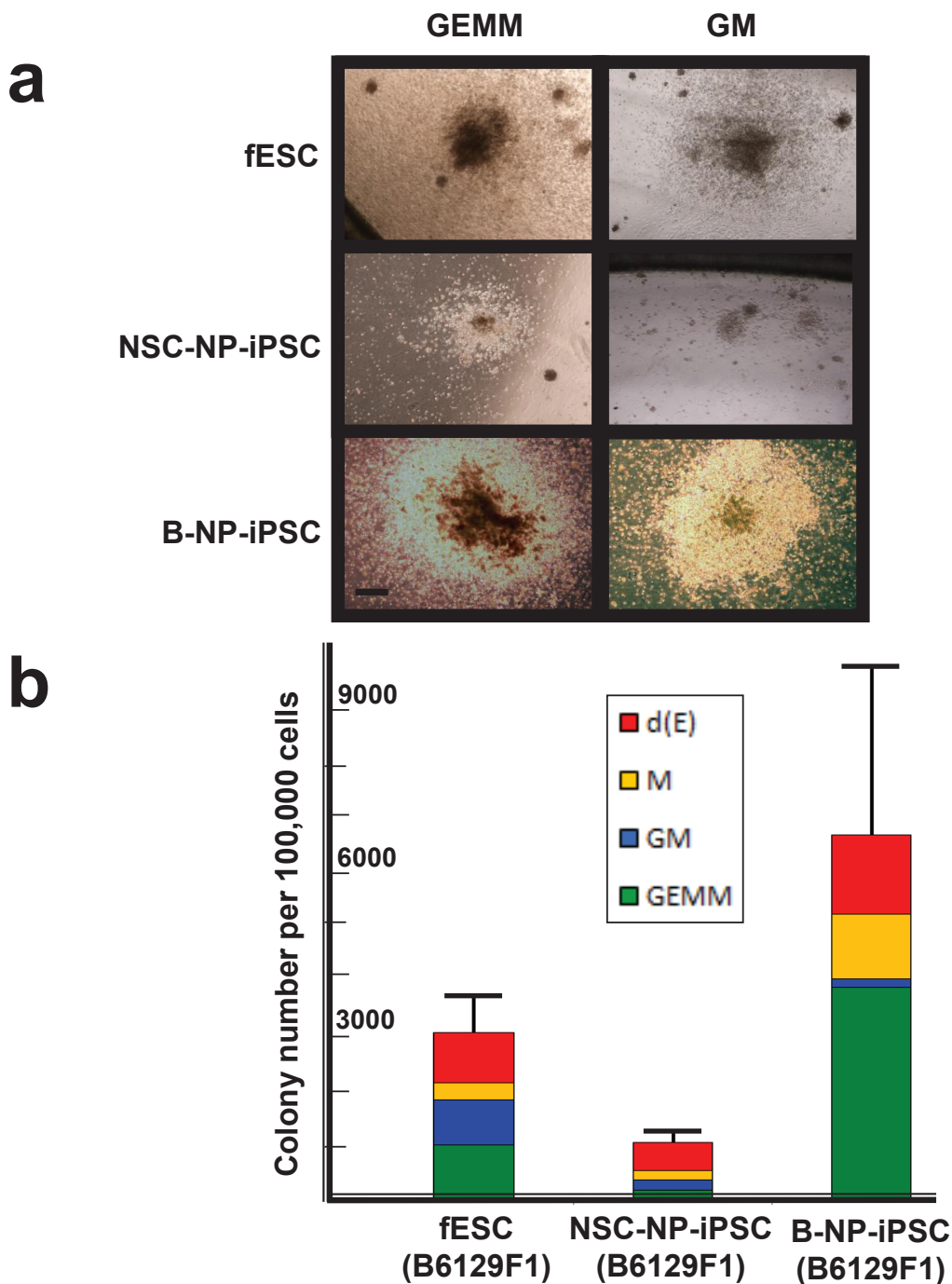


**ntESC chimera and germ line transmission**



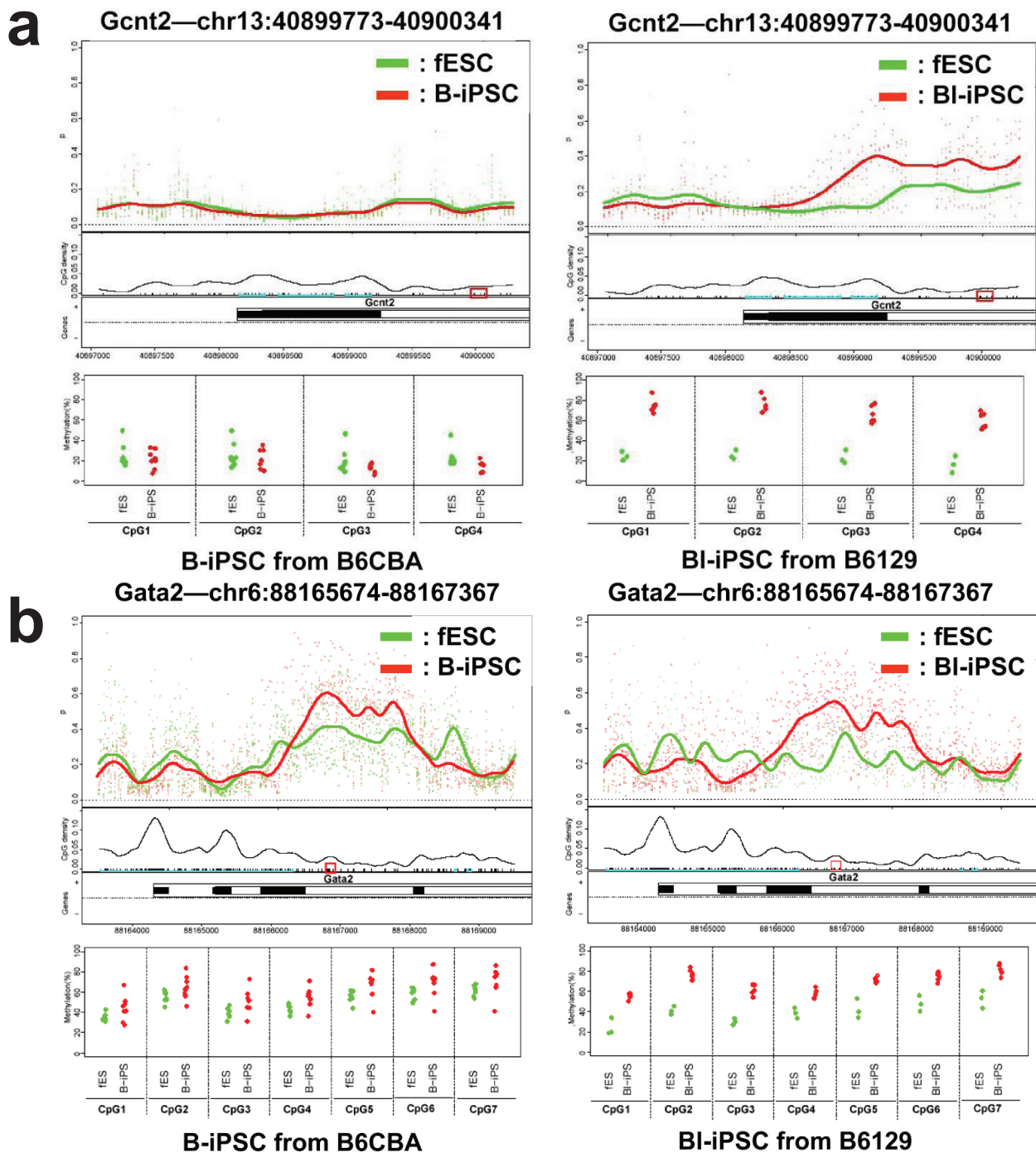
**B-NP-iPSC chimera    NSC-NP-iPSC chimera**

Supplementary Figure 9 | Mouse chimerism and germ line transmission of the fESC, ntESC, B-NP-iPSC, and NSC-NP-iPSC (refer to Fig. 4a).

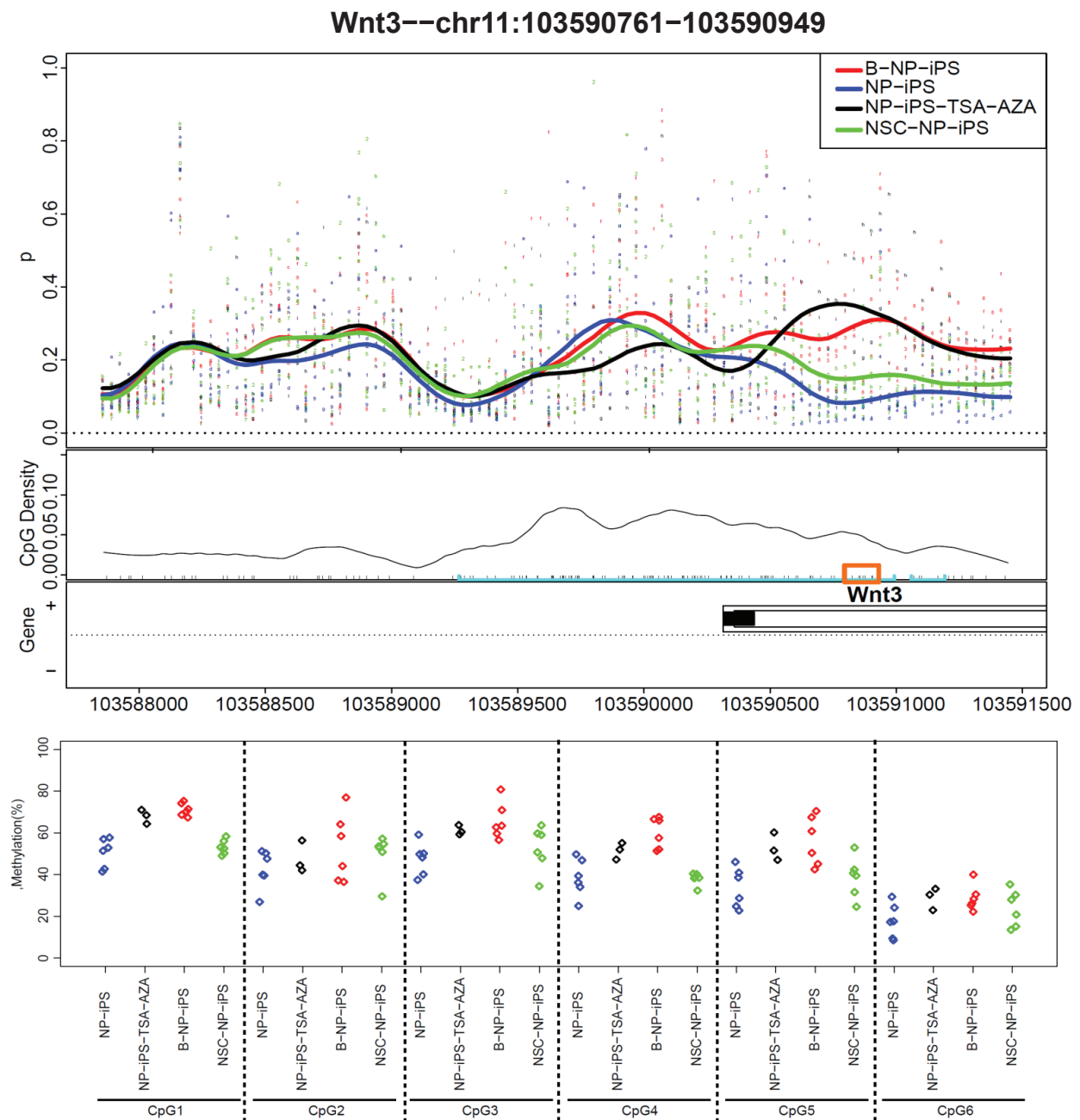


**Supplementary Figure 10 | Hematopoietic colony formation by fESC, NSC-NP-iPSC, and B-NP-iPSC. a,** Different sizes of GEMM and GM colonies in methylcellulose cultures of fESC, NSC-NP-iPSC, and B-NP-iPSC. (40X magnification). Scale bar, 500 $\mu$ m. **b,** Average cell number per colony among 20 randomly picked colonies from fESC, NSC-NP-iPSC, and B-NP-iPSC. Error bars = s.d.

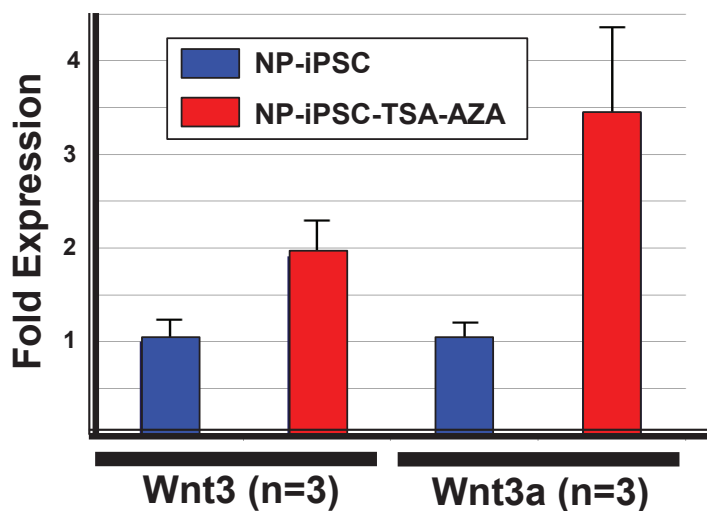
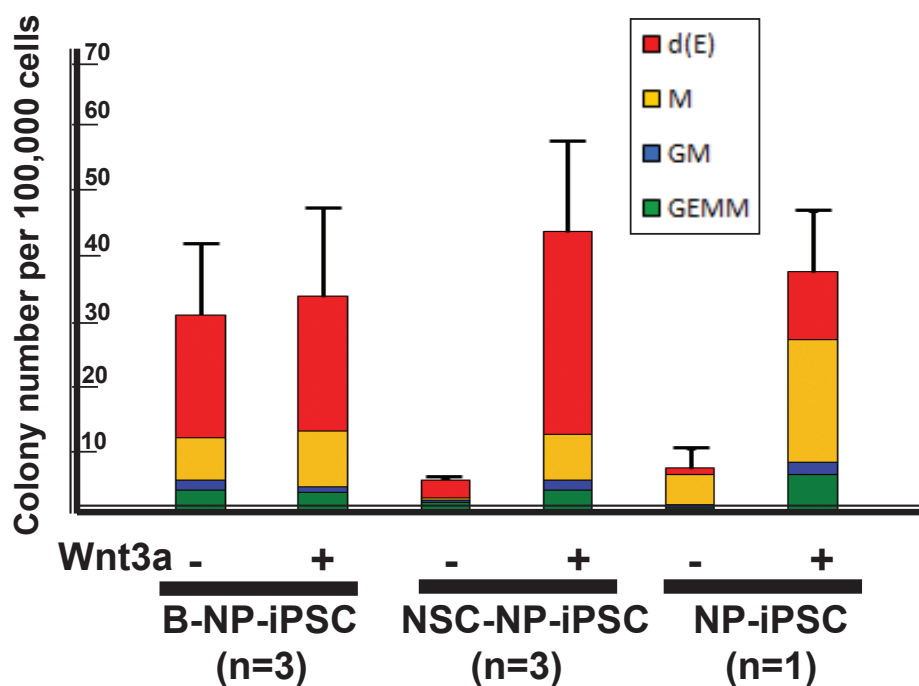




**Supplementary Figure 11 | Residual DNA methylation at hematopoiesis-related loci. a, *Gcnt2* and b, *Gata2* genes show a greater degree of hypermethylation in BI-iPSC relative to fESC compared to B-iPSC vs fESC. Upper panels show CHARM plots, while lower panels represent the degree of DNA methylation (of the CpG sites indicated in the red box in the upper panels) as measured by bisulfite pyrosequencing.**



**Supplementary Figure 12 | DNA methylation at Wnt3.** iPSCs that have higher hematopoietic potential (B-NPiPSC and NP-iPSC-TSA-AZA) show a greater degree of Wnt3 gene body methylation<sup>3</sup> than the iPSCs that have lower hematopoietic potential (NSC-NPiPSC and NP-iPSC). Upper panel shows CHARM plots, while lower panel represents the degree of DNA methylation as measured by bisulfite pyrosequencing. The orange box indicated on the x axis of the CpG density plot in the upper panel marks the CpG sites that were measured by bisulfite pyrosequencing.

**a****b**

**Supplementary Figure 13 | Relationship of Wnt3/3a on hematopoietic potential of NP-iPSC and NSC-NP-iPSC.** **a**, RNA from EBs differentiated for 3 days were harvested and analyzed by quantitative PCR, after normalization to  $\beta$ -actin. Numbers represent fold expression of NP-iPSC-TSA-AZA (red bar) relative to NP-iPSC (blue bar). **b**, Methylcellulose analysis of blood-forming potential of iPSCs with Wnt3a treatment (+) between day 2-4 of EB differentiation compared to non-treated EBs (-). Error bars = s.d.



**a**

Comparison	Number of DMRs	Methylation	Number of DMRs
fESC vs. F-iPSC	5304	fESC>F-iPSC	1955
		fESC<F-iPSC	3349
fESC vs. B-iPSC	694	fESC>B-iPSC	178
		fESC<B-iPSC	516
fESC vs. ntESC	229	fESC>ntESC	173
		fESC<ntESC	56
F-iPSC vs. B-iPSC	5202	F-iPSC>B-iPSC	2850
		F-iPSC<B-iPSC	2352
F-iPSC vs. ntESC	6255	F-iPSC>ntESC	4077
		F-iPSC<ntESC	2178
B-iPSC vs. ntESC	995	B-iPSC>ntESC	897
		B-iPSC<ntESC	98

*\*area cutoff of 2.0.*

**b**

Comparison	Number of DMRs	Methylation	Number of DMRs
BI-iPSC vs. fESC	1485	BI-iPSC>fESC	1423
		BI-iPSC<fESC	62
BI-iPSC vs. NP-iPSC	2344	BI-iPSC>NP-iPSC	2326
		BI-iPSC<NP-iPSC	18
BI-iPSC vs. ntESC	3053	BI-iPSC>ntESC	3000
		BI-iPSC<ntESC	53
fESC vs. NP-iPSC	553	fESC>NP-iPSC	136
		fESC<NP-iPSC	417
fESC vs. ntESC	679	fESC>ntESC	399
		fESC<ntESC	280
NP-iPSC vs. ntESC	571	NP-iPSC>ntESC	469
		NP-iPSC<ntESC	102

*\*area cutoff of 2.0.*

**c**

Comparison	Number of DMRs	Methylation	Number of DMRs
NP-iPSC vs. NSC-NP-iPSC	107	NP-iPSC>NSC-NP-iPSC	46
		NSC-NP-iPSC>NP-iPSC	61
NP-iPSC vs. B-NP-iPSC	803	NP-iPSC>B-NP-iPSC	593
		B-NP-iPSC>NP-iPSC	210
NP-iPSC vs. NP-iPSC-TSA-AZA	938	NP-iPSC	626
		>NP-iPSC-TSA-AZA	
		NP-iPSC-TSA-AZA	312
NSC-NP-iPSC vs. B-NP-iPSC	688	>NP-iPSC	
		NSC-NP-iPSC	632
		>B-NP-iPSC	
		B-NP-iPSC	56
		>NSC-NP-iPSC	

*\* area cutoff of 2.0.*

**Supplementary Table 1 | . DMRs by CHARM analysis. a**, fESC, ntESC, B-iPSC, and F-iPSC (refer to Fig. 1a), **b**, fESC, ntESC, NP-iPSC, and BI-iPSC (refer to Fig. 4a upper schema), **c**, NP-iPSC, NSC-NP-iPSC, NP-iPSC-TSA-AZA, and B-NP-iPSC (refer to Fig. 4a lower schema).

Rank	Gene	Function	Reference
1	Kcnrg		
2	Mast1		
3	Mab21L1	Osteogenetic differentiation	4
4	Atbf1	Myb mediated hematopoietic growth regulation	5
5	Hand1	Cardiac development	6
6	Zfp423	Enhance Hematopoietic activity	7
7	Pcdhga10	protocadherin	8
8	Dlx1	Hematopoietic development with BMP4	9
9	Pim1	Hematopoietic proliferation	10
10	Efnb2	Developmental events, especially in the nervous system and in erythropoiesis	11
11	Asns	Hematopoietic proliferation	12
12	Tradd	programmed cell death	13
13	Ebf2	Osteogenetic differentiation	14
14	Slc13a4	Sodium/sulfate cotransporter	15
15	Osr2	Osteogenetic development	16
16	Igsf4c	Immunoglobulin superfamily	17
17	Meis1	Definitive hematopoiesis	18
18	CD37	T cell B cell interaction and proliferation	19 20
19	Slc38a4		
20	Pcdhga12	Protocadherin	8
21	Pcdhga7	Protocadherin	8
22	Map2k7	Hematopoietic growth	21
23	Sall4	Bmi-1 mediated hematopoietic self-renewal	22
24	Pcdhgb6	Protocadherin	8

**Supplementary Table 2 | Top 24 Differentially Methylated Regions (DMRs) between B-iPSC and F-iPSC.** Blood-related genes are shaded in red; bone-related genes are shaded in light brown.

aff1	ccnk	gas7	irf1	irf8	myc	runx1	sp4	zfp3611
arhgap17	elf1	hhex	irf2	klf6	nfe2l2	runx3	stat1	
bcl3	etv3	ifnar2	irf5	lyl1	rbl1	sirt7	stat6	
bcor	fli1	ikbkb	irf7	mtpn	rela	smad2	zfp182	

Supplementary Table 3 | Hematopoiesis-related transcription factors that are differentially methylated in F-iPSC vs B-iPSC (Fig. 1a), NP-iPSC vs BI-iPSC (Fig. 4a upper schema), and/or NSC-NP-iPSC vs B-NP-iPSC (Fig. 4a lower schema).



Methylation		DN3 > MPP <sup>FL-</sup> (496)	DN3 < MPP <sup>FL-</sup> (237)	GMP > MPP <sup>FL-</sup> (177)	GMP < MPP <sup>FL-</sup> (567)	DN3 > GMP (706)	DN3 < GMP (207)
DMRs between B-iPSC and fESC (B6/CBA; B-iPSC derived from Kit+, lineage-negative myeloid marrow precursors)	B-iPSC > fESC (516)	10	3	7	2	5	3
	B-iPSC < fESC (178)	2	1	0	5	0	0
DMRs between BI-iPSC and fESC (B6/129; BI-iPSC derived from B lymphocytes )	BI-iPSC > fESC (1423)	20	13	6	20	31	6
	BI-iPSC < fESC (62)	0	0	0	0	0	0

DN3 is T cell lineage committed  
GMP is myeloid lineage committed  
Flk2<sup>+</sup> is the multipotent progenitor

**Supplementary Table 4 | Comparison of DMRs that distinguish MPP<sup>FL-</sup> from DN3, MPP<sup>FL-</sup> from GMP, and DN3 from GMP, with two groups of blood-derived iPSC (B-iPSC and BI-iPSC) compared to fESC.** Multiple comparisons were made to ascertain any correlation in the direction of DNA methylation changes from the two sets of data. MPP (multipotent progenitors), CLP (common lymphoid progenitors), CMP (common myeloid progenitors), GMP (granulocyte/monocyte progenitors), and DN3 (thymocyte progenitors).

Cut AREA: 5	Genes	DMRs in B6/CBAF1 mouse (refer to Fig. 1a)		
Number of Common target		fESC vs ntESC	fESC vs B-iPSC	fESC vs F-iPSC
7 Core factor	47	0	0	11
6 Core factor	100	0	1	25
5 Core factor	124	0	1	24
4 Core factor	227	0	2	42
3 Core factor	427	0	0	56
2 Core factor	901	0	4	143
1 Core factor	2350	2	16	332
0 Core factor	9686	14	79	1077
<b>Total DMRs</b>	<b>13862</b>	<b>16</b>	<b>103</b>	<b>1710</b>

Cut AREA: 5	Genes	DMRs in B6/129F1 mouse (refer to Fig. 4a upper schema)		
Number of Common target		fESC vs ntESC	fESC vs NP-iPSC	fESC vs BI-iPSC
7 Core factor	47	0	0	1
6 Core factor	100	2	2	3
5 Core factor	124	0	0	3
4 Core factor	227	1	2	7
3 Core factor	427	4	3	11
2 Core factor	901	6	6	22
1 Core factor	2350	13	13	49
0 Core factor	9686	34	53	189
<b>Total DMRs</b>	<b>13862</b>	<b>60</b>	<b>79</b>	<b>285</b>

**Supplementary Table 5 | DMRs and pluripotency network genes defined by fESC core factor co-occupancy.** Correlation between seven core factor co-occupancy on their target genes<sup>23</sup> and DMRs generated from each comparison set were tested to define the functionally linked DMRs in pluripotent network genes. Core factors tested in this analysis are Nanog, Sox2, Oct4, Klf4, Dax1, Nac1, and Zfp281, and the number of DMRs found in each gene set defined by target co-occupancy (by 7 TFs to 0 TF) is shown.

**Supplementary Table 6 | List of pluripotent stem cells and their characterization.** A "xxx" represents a relative degree of expression level or demethylation level. Blank indicates "not determined". "Yes" indicates "confirmed". Germ cell transmission was determined as follows: Birth of marked pups from mating of chimeric animals is indicated "Yes"; birth of pups following tetraploid embryo complementation is indicated "4N complementation"; detection of donor-marked SSEA1+ presumptive germ cells isolated from the gonadal ridge of chimeric embryos, as determined by flow cytometry is indicated as "Yes (gonad)".  $\beta$  symbol in donor tissue type indicates "carries beta thal deletion".

cell line	Tissue donor stain	donor tissue type	passage number	teratoma formation	Oct4 transcription	Nonog transcription	Oct4 promoter demethylation	Nanog promoter demethylation	immunohistochemistry Oct4/Nanog	chimera	germ cell transmission
<b>iESC</b>											
iESC-A	B6CBAF1	blastocyst	3 ~ 7	xxx							
iESC-B	B6CBAF1	blastocyst	3 ~ 7	xxx							
iESC-C	B6CBAF1	blastocyst	3 ~ 7	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes
iESC-D	B6CBAF1	blastocyst	3 ~ 7	xxx							
iESC-E	B6CBAF1	blastocyst	3 ~ 7	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes
iESC-F	B6CBAF1	blastocyst	3 ~ 7	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes
iESC-G	B6CBAF1	blastocyst	3 ~ 7	xxx							
iESC-I	B6CBAF1	blastocyst	3 ~ 7	xxx							
iESC-PGEE2-1	B6129F1	blastocyst	3 ~ 6	xxx						Yes	Yes
iESC-PGEE2-2	B6129F1	blastocyst	3 ~ 6	xxx						Yes	Yes
iESC-V6.5	B6129F1	blastocyst	9 ~ 11	xxx		xxx	xxx	xxx	xxx	Yes	Yes (4n complementation)
<b>ntESC</b>											
ntESC-B1	B6CBAF1	fibroblast	3 ~ 7	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes
ntESC-B3	B6CBAF1	fibroblast	3 ~ 7	xxx							
ntESC-F1	B6CBAF1	fibroblast	3 ~ 7	xxx							
ntESC-O	B6CBAF1	fibroblast	3 ~ 7	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes
ntESC-V1	B6CBAF1	fibroblast	3 ~ 7	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes
ntESC-V2	B6CBAF1	fibroblast	3 ~ 7	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes
ntESC-V3	B6CBAF1	fibroblast	3 ~ 7	xxx							
ntESC-NGFP	B6129F1	embryonic fibroblast	11	xxx						Yes	Yes (4n complementation)
ntESC-LN1	B6D2F1	B cell	5 ~ 8	xxx						Yes	Yes (4n complementation)
ntESC-LN2	B6129F1	T cell	5 ~ 8	xxx						Yes	Yes (4n complementation)
ntESC-LN3	B6129F1	T cell	5 ~ 8	xxx						Yes	Yes (4n complementation)
ntESC-Rag2	B6129F1	fibroblast	5 ~ 8	xxx						Yes	Yes (4n complementation)
ntESC-V6.5NSCB1	B6129F1	neural stem cell	5 ~ 8	xxx						Yes	Yes (4n complementation)
ntESC-V6.5NSCB2	B6129F1	neural stem cell	5 ~ 8	xxx						Yes	Yes (4n complementation)

cell line	Tissue donor stain	donor tissue type	passage number	teratoma formation	Oct4 transcription	Nonog transcription	Oct4 promoter demethylation	Nanog promoter demethylation	immunohistochemistry Oct4/Nanog	chimera	germ cell transmission
<b>iPSC</b>											
F-IPSC1	B6BAF1	fibroblast $\beta$	3 ~ 7	xxx	xxx	xx	xxx	xxx	xxx	Yes	Yes (gonad)
F-IPSC13	B6BAF1	fibroblast $\beta$	3 ~ 7	xxx	xxx	xx	xxx	xxx	xxx	Yes	Yes (gonad)
F-IPSC16	B6BAF1	fibroblast $\beta$	3 ~ 7	xxx	xxx	xx	xxx	xxx	xxx	Yes	Yes (gonad)
F-IPSC34	B6BAF1	fibroblast $\beta$	3 ~ 7	xxx							
F-IPSC36	B6BAF1	fibroblast $\beta$	3 ~ 7	xxx							
F-IPSC37	B6BAF1	fibroblast $\beta$	3 ~ 7	xxx							
F-IPSC39	B6BAF1	fibroblast $\beta$	3 ~ 7	xxx							
F-IPSC63	B6BAF1	fibroblast $\beta$	3 ~ 7	xxx							
B-IPSC2	B6BAF1	hematopoietic cell $\beta$	3 ~ 7	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes (gonad)
B-IPSC6	B6BAF1	hematopoietic cell $\beta$	3 ~ 7	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes (gonad)
B-IPSC8	B6BAF1	hematopoietic cell $\beta$	3 ~ 7	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes (gonad)
B-IPSC10	B6BAF1	hematopoietic cell $\beta$	3 ~ 7	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes (gonad)
B-IPSC11	B6BAF1	hematopoietic cell $\beta$	3 ~ 7	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes (gonad)
B-IPSC12	B6BAF1	hematopoietic cell $\beta$	3 ~ 7	xxx							
B-IPSC15	B6BAF1	hematopoietic cell $\beta$	3 ~ 7	xxx							
B-IPSC16	B6BAF1	hematopoietic cell $\beta$	3 ~ 7	xxx							
B-IPSC18	B6BAF1	hematopoietic cell $\beta$	3 ~ 7	xxx							
BI-IPSC-ABiPS	B6129F1	B cell	6 ~ 8	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes
BI-IPSC-E2-1	B6129F1	B cell	6 ~ 8	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes
BI-IPSC-K02-2	B6129F1	B cell	6 ~ 8	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes
BI-IPSC-K01-2	B6129F1	B cell	6 ~ 8	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes
BI-IPSC-BiPS54	B6129F1	B cell	6 ~ 8	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes
BI-IPSC-E3-1	B6129F1	B cell	6 ~ 8	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes
NP-IPSC0	B6129F1	neural progenitor cell	6 ~ 8	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes
NP-IPSC1	B6129F1	neural progenitor cell	2 ~ 5	xxx	xxx	xxx	xxx	xxx	xxx		
NP-IPSC2	B6129F1	neural progenitor cell	2 ~ 5	xxx	xxx	xxx	xxx	xxx	xxx		
NP-IPSC3	B6129F1	neural progenitor cell	2 ~ 5	xxx	xxx	xxx	xxx	xxx	xxx		
NP-IPSC4	B6129F1	neural progenitor cell	2 ~ 5	xxx	xxx	xxx	xxx	xxx	xxx		
NP-IPSC5	B6129F1	neural progenitor cell	2 ~ 5	xxx	xxx	xxx	xxx	xxx	xxx		
NP-IPSC6	B6129F1	neural progenitor cell	2 ~ 5	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes
NSC-NP-IPSC1	B6129F1	NPiPS-neural stem cell	2 ~ 5	xxx	xxx	xxx	xxx	xxx	xxx		
NSC-NP-IPSC2	B6129F1	NPiPS-neural stem cell	2 ~ 5	xxx	xxx	xxx	xxx	xxx	xxx		
NSC-NP-IPSC3	B6129F1	NPiPS-neural stem cell	2 ~ 5	xxx	xxx	xxx	xxx	xxx	xxx		
NSC-NP-IPSC4	B6129F1	NPiPS-neural stem cell	2 ~ 5	xxx	xxx	xxx	xxx	xxx	xxx		
NSC-NP-IPSC5	B6129F1	NPiPS-neural stem cell	2 ~ 5	xxx	xxx	xxx	xxx	xxx	xxx		
NSC-NP-IPSC6	B6129F1	NPiPS-neural stem cell	2 ~ 5	xxx	xxx	xxx	xxx	xxx	xxx		
NP-IPSC-TSA-AZA1	B6129F1	NPiPS-neural stem cell	2 ~ 3	xxx	xxx	xxx	xxx	xxx	xxx		
NP-IPSC-TSA-AZA2	B6129F1	NPiPS-neural stem cell	2 ~ 3	xxx	xxx	xxx	xxx	xxx	xxx		
NP-IPSC-TSA-AZA3	B6129F1	NPiPS-neural stem cell	2 ~ 3	xxx	xxx	xxx	xxx	xxx	xxx		
B-NP-IPSC14-1	B6129F1	NPiPS-blood lineage	2 ~ 5	xxx	xxx	xxx	xxx	xxx	xxx	Yes	Yes
B-NP-IPSC15-1	B6129F1	NPiPS-blood lineage	2 ~ 5	xxx	xxx	xxx	xxx	xxx	xxx		
B-NP-IPSC15-2	B6129F1	NPiPS-blood lineage	2 ~ 5	xxx	xxx	xxx	xxx	xxx	xxx		
B-NP-IPSC1	B6129F1	NPiPS-blood lineage	2 ~ 5	xxx	xxx	xxx	xxx	xxx	xxx		
B-NP-IPSC2	B6129F1	NPiPS-blood lineage	2 ~ 5	xxx	xxx	xxx	xxx	xxx	xxx		
B-NP-IPSC3	B6129F1	NPiPS-blood lineage	2 ~ 5	xxx	xxx	xxx	xxx	xxx	xxx		



Gene	Primer	Sequence (5' → 3')	Chromosomal Coordinates					
			Chr	CG1	CG2	CG3	CG4	CG5
<i>Pou5f1</i> ( <i>Oct4</i> )	Forward	GTTGTTTGGTTTTGGTTTTGGATAT						
	Reverse	CAAAAAACCTTCATTTTCAACCTT						
	Nested forward	TGAGGAGTGGTTTTAGAAATAATTG						
	Nested reverse	/5Biosg/AATCCTCTCACCCCTACCTAAAT						
	Sequencing1 (F) Sequencing2 (F)	TGAGGAGTGGTTTTAGAAATAATTG GAGGGGTAGTGTTAATAGGTTTTG	chr17	35113732	35113827	35113839	35113863	
<i>Nanog</i>	Forward	GTAATAGAGAAAAATTTGTTTTAAATTA						
	Reverse	CTACAAACATAAAAAATCAAACCT						
	Nested forward	TTTAAGTAGGATATAGGTTTTTTTT						
	Nested reverse	/5Biosg/ACTACCAAAATCTCTATTATACAC						
	Sequencing 1 (F) Sequencing 2 (F)	TTTAAGTAGGATATAGGTTTTTTTT TTAATGTGAAGAGTAAGTAAGAAA	chr6	122672685	122672696	122672753	122672775	
<i>Cd37</i>	Forward	AGATGTGAGTTTTGTAGGGAGTGTATA						
	Reverse	CATATTCTTAATCCCTAAACCCCAT						
	Nested forward	TTTAGTTGGGAGAAAAAGAGTTTATTTAA						
	Nested reverse Sequencing (F)	/5Biosg/CAAACCTAACTACACACCTACACC TTTTTAGTATTTGGGTTTTGTTTTA	chr7	45103657	45103659	45103673	45103681	
<i>Kcnrg</i>	Forward	TAATTTGTATGGAGAGTTTGGTTTG						
	Reverse	CCCCAATTATATTTAATTACCTTCAC						
	Nested forward	TTTGTAGAAGTAAAGGAGTGTGATA						
	Nested reverse Sequencing (F)	/5Biosg/TCACTACAATAACTCTATAAAAAAAA TGGTAGATGTTTAGTAGGGTTTTAG	chr14	60638814	60638820	60638828	60638848	60638857
<i>Rest</i>	Forward	TGGGAGATAATTATTTTTAGAAAGTGA						
	Reverse	TCCCAAACTTTAACTATTTCTCTACA						
	Nested forward	TTGATTTTAAAGGTTGGAAAATAT						
	Nested reverse Sequencing (F)	/5Biosg/AAAACCTTAACTTAAACTCTACA AAGTTTTAGTTGTTTAGAAATA	chr5	78343105	78343120	78343135	78343140	
<i>Slc32a1</i>	Forward	TTTGGTTGATTTTTAGGAATTATT						
	Reverse	AAAAACAACCCCAATAACC						
	Nested forward	TTGTGAGATTTTTATTTTTTTTT						
	Nested reverse Sequencing (F)	/5Biosg/ACCAAACCCAAAACTCAACTAAT TTTTTTGATTTAATATTTAGA	chr2	158305089	158305106	158305128		
<i>Oct4</i>	Forward	AGCTGCTGAAGCAGAAGAGGATCATCTCATT	QPCR					
	Reverse	GTTGTCGGCTTCCTCCA	Primer					
<i>Nanog</i>	Forward	AACCAAGGATGAAGTGCAAGCGGTCCAAG	QPCR					
	Reverse	TTGGGTTGGTCCAAGTCT	Primer					
<i>Actin</i>	Forward	TGAAGTGTGACGTGGACATC	QPCR					
	Reverse	GGAGGAGCAATGATCTTGA	Primer					

/5Biosg/ = 5' biotin added, F = forward

**Supplementary Table 7 | Primer sequences used for bisulfite pyrosequencing and rtPCR.**  
The chromosomal coordinates for the locations of CpG sites interrogated in the bisulfite pyrosequencing are based on the UCSC Genome Browser Mouse Feb. 2006 Assembly (mm8).

Hematopoietic Transcription Factors									
aff1	ankfy1	arhgap17	atf3	batf	bcl3	bcor	ccnk	creb1	creg1
dazap2	dmtf1	dpf2	dr1	elf1	elk4	etv3	fli1	gas7	gmeb1
hhex	htatip2	ifi204	ifnar2	ikbkb	ikbkg	ikzf1	ikzf3	ints12	irf1
irf2	irf5	irf7	irf8	klf6	limd1	lyl1	mtpn	myb	myc
nfatc1	nfe2l2	nfkbl	nfkblie	nfya	nmi	ostf1	papola	papolg	pcbd2
plagl2	rab8a	rab8b	rbl1	rcor1	rel	rela	runx1	runx3	sertad1
sirt7	smad2	sp4	stat1	stat4	stat5a	stat6	tal1	tceb3	tnfaip3
zfp182	zfp36	zfp36l1	zfp426						

**Supplementary Table 8 | List of Hematopoietic Transcription Factors (Cahan and Daley, unpublished), applied in the gene enrichment analysis in Fig. 3b and Supplementary Fig. 3c.**

Fibroblast Specific Genes					
1110012d08rik	1110036o03rik	1200002n14rik	1200009f10rik	1300014i06rik	1810037c20rik
2310038h17rik	2310047d13rik	2610034b18rik	2810022i02rik	2810055f11rik	2900026a02rik
3110032g18rik	9030425e11rik	9130005n14rik	9430028i06rik	9930013i23rik	a130022j15rik
abca1	abi3bp	aco1	acvr1	acvr1	adam12
adam19	adam33	adam9	adamts1	adamts10	adamts12
adamts5	adamts1	adamts15	adcy4	adm	aebp1
agtr1a	ai597468	akap2	aldh112	alg14	angpt12
ankrd1	antxr1	aqp1	arfgap1	arhgap28	arhgef19
arsj	asah2	atf5	atp11a	avpr1a	aw061290
aw548124	axl	b4galt4	bag2	bambi	bc029169
bc035537	bgn	bicc1	bicd2	bmp1	bmp5
bmpcr	boc	c130021i20rik	c1qtnf2	c1qtnf3	c1qtnf5
c1qtnf6	c1s	c2	calcoco1	calu	capn6
cask	casp12	cav1	cbr2	ccdc102a	ccdc68
cd248	cd276	cdc16	cdc42ep1	cdc42ep2	cdh11
cdkn1c	cdkn2b	cdon	cebpb	cfh	cgln1
chac1	chmp2b	chr11	ckap4	cldn1	clec11a
clec14a	clic4	cnn1	col11a1	col14a1	col15a1
col16a1	col1a1	col1a2	col27a1	col2a1	col5a1
col5a3	col6a1	col6a2	col7a1	col8a1	col8a2
col9a1	col9a2	colec12	copz2	cp	cpa6
cpne8	cpxm1	cpxm2	cpz	crabp1	crabp2
creb3	creb3l2	crim1	crim2	crispld2	crlf1
csf1	cspg4	ctdspi	cthr1	ctps	ctsl
cxcl12	cxcl14	cxcl5	cyp1b1	cyp26b1	cyr61
d10ertd610e	d4bwg0951e	dab2	dcn	ddr2	dkk2
dkk3	dmpk	dpysl3	dysf	e130203b14rik	e430002g05rik
ebf1	ebf2	ece1	ednra	efemp2	efna4
efna5	efnb1	egr	ehd2	eln	emid2
emp2	emx2	en1	entpd2	epha3	ephb2
ephx1	errfi1	evi1	ext1	eya4	fads3
fap	farp2	fat4	fbln1	fbln2	fbln5
fbn1	fbn2	fbxl7	fbxo17	fcgrt	fez2
fgf18	fgf2	fgfr2	fgfr1	fhl2	figf
fkbp10	fkbp14	flrt2	flt1	fmod	fn1
fndc3b	fosl1	foxc1	foxc2	foxd1	frmd6
frs2	fst	fstl3	fzd1	fzd2	fzd6
fzd8	gadd45g	gal3st4	galnt14	gas1	gas6
gata6	gdnf	ggcx	ghr	gjb2	glce
gli3	glis1	glis3	glit1d2	gm106	gng11

Supplementary Table 9 | List of Fibroblast Specific Genes (Cahan and Daley, unpublished), applied in the gene enrichment analysis in Fig. 3b.

Fibroblast Specific Genes					
gng12	gng8	golga3	gpc1	gpc6	gpr124
gpr176	gpr180	gpx3	gpx7	grb10	grem1
grem2	gulp1	h1f0	has2	hcfc1r1	hebp2
hey1	hgf	hhat	hic1	hist1h1c	hist1h2bc
hist2h3c1	hoxa11	hoxa2	hoxb2	hoxb6	hoxc8
hoxd10	hoxd8	hoxd9	hs2st1	hspa12b	hspa1b
hsqb8	htra3	id3	igf1	igf2	igf2r
igfbp3	igfbp4	il13ra1	il1r1	il6st	il7
ilk	irx1	irx2	irx3	irx5	islr
itfg3	itga1	itga8	itgb5	kazald1	kcne4
kcnj8	kctd11	kctd12b	kdelr3	lama2	lama4
laptm4a	lect1	lepre1	lepre1	lepre2	lgals7
lgr5	lhfp	lmcd1	lmod1	lox	lox1
lox12	lox13	lox14	lrp1	lrp6	lrrc15
lrrc41	lrrc58	ltbp1	ltbp2	ltbp3	ly6a
lzts2	maf	mamdc2	marcks	masp1	matn2
matn4	mcam	meox1	meox2	mertk	mfap2
mfap4	mfap5	mfge8	mgst1	mical2	mid2
mkx	mmp11	mmp14	mmp2	morc4	mr1
mrc2	mrgprf	msrb3	msx1	msx2	mtmr11
mxra8	mylk	nab2	nbl1	ncbp2	nenf
net1	nexn	nfatc4	nfil3	nfix	nkd1
nkd2	npnt	npr2	npr3	nr2f2	nt5e
ntn4	nuak1	nudt6	nxn	oaf	oat
olfml1	olfml2a	olfml2b	ormdl3	osbp15	osmr
osr1	p4ha2	p4ha3	pappa	pard6g	pbxip1
pcdh18	pcdh7	pcdhb22	pcyox1	pde3a	pdgfd
pdgfra	pdgfrb	pdgfrl	pdia5	pdpn	pdzd11
pdzrn3	pgf	pgm5	phlda3	phldb1	plagl1
plekhf1	plekhh2	pmp22	podn	ppic	prelp
prkcdbp	prkg1	prrx2	prss23	prss35	pthr1
ptk7	ptpla	ptpn9	ptrf	ptx3	qpctl
rassf8	rbms3	rcn1	rcn3	reck	reg
rgs3	rhobtb3	rhoj	rhoq	rin2	rnase4
rnd3	ror1	ror2	rspo3	samd4	scara3
scara5	scarf2	scube2	scx	scyl1	sdc4
sdpr	sec22b	sema3c	sema3d	sepn1	serpina3n
serpinf1	sfrp2	sfrp4	sgcd	six5	slc10a6
slc16a4	slc2a10	slc35f5	slc39a13	slco2a1	slit3
smad1	smad3	smad5	smad6	smo	smoc2

Supplementary Table 9 | List of Fibroblast Specific Genes-Continued

Fibroblast Specific Genes					
smpd2	smtn	snai1	snai2	sned1	sorbs3
sox4	spg20	sphk1	spon2	spsb1	sqrdl
sspn	st5	stard13	stau1	steap1	sulf1
svep1	tagln	tbc1d19	tbx18	tbx2	tcf21
tcf7l2	tenc1	tfpi2	tgfb1i1	tgfb2	tgfb3
tgfbr3	tgm2	thbd	thbs1	thbs2	timp2
tll1	tm9sf3	tmbim1	tmcc3	tmem119	tmem159
tmem16a	tmem16k	tmem176a	tmem176b	tmem5	tmem65
tmem86a	tmem98	tmtc4	tnc	tnfaip1	tnfrsf12a
tnmd	tnn	tnxb	tpm1	tspan31	tspan6
twist1	twist2	ube2r2	unc5b	vasn	vcam1
vegfa	vnn1	wipi1	wisp1	wnt5a	yipf5
zcchc5	zfand3	zfhx4	zfp275	zfp449	zfp503
zfp521	zfp637	zfp647	zfp9		

Supplementary Table 9 | List of Fibroblast Specific Genes-Continued



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