SUPPLEMENTAL INFORMATION

Supplemental information includes five figures and 1 table.

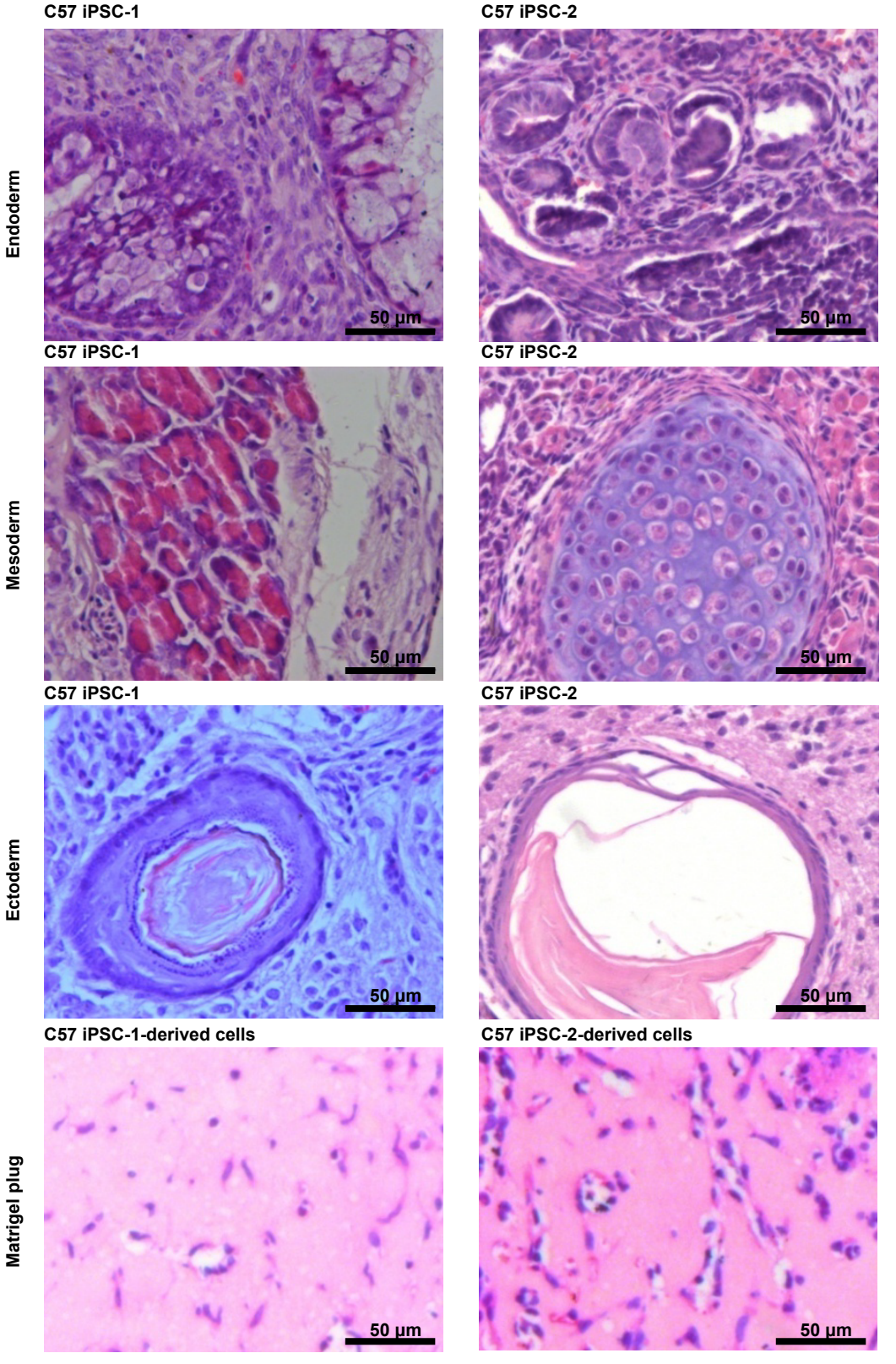


Figure S1. Histological analyses of teratomas formed in syngeneic mice generated from subcutaneously injected mouse iPSCs. The teratoma tissues were stained using hematoxylin and eosin to identify cells originating from the three germ layers (top three panels): endocrine glands (endoderm), muscle and cartilage (mesoderm), and epidermis (ectoderm). The lower panel shows the Matrigel plug harvested 28 days after subcutaneous injection of Matrigel-suspended mouse iPSC-derived cells.

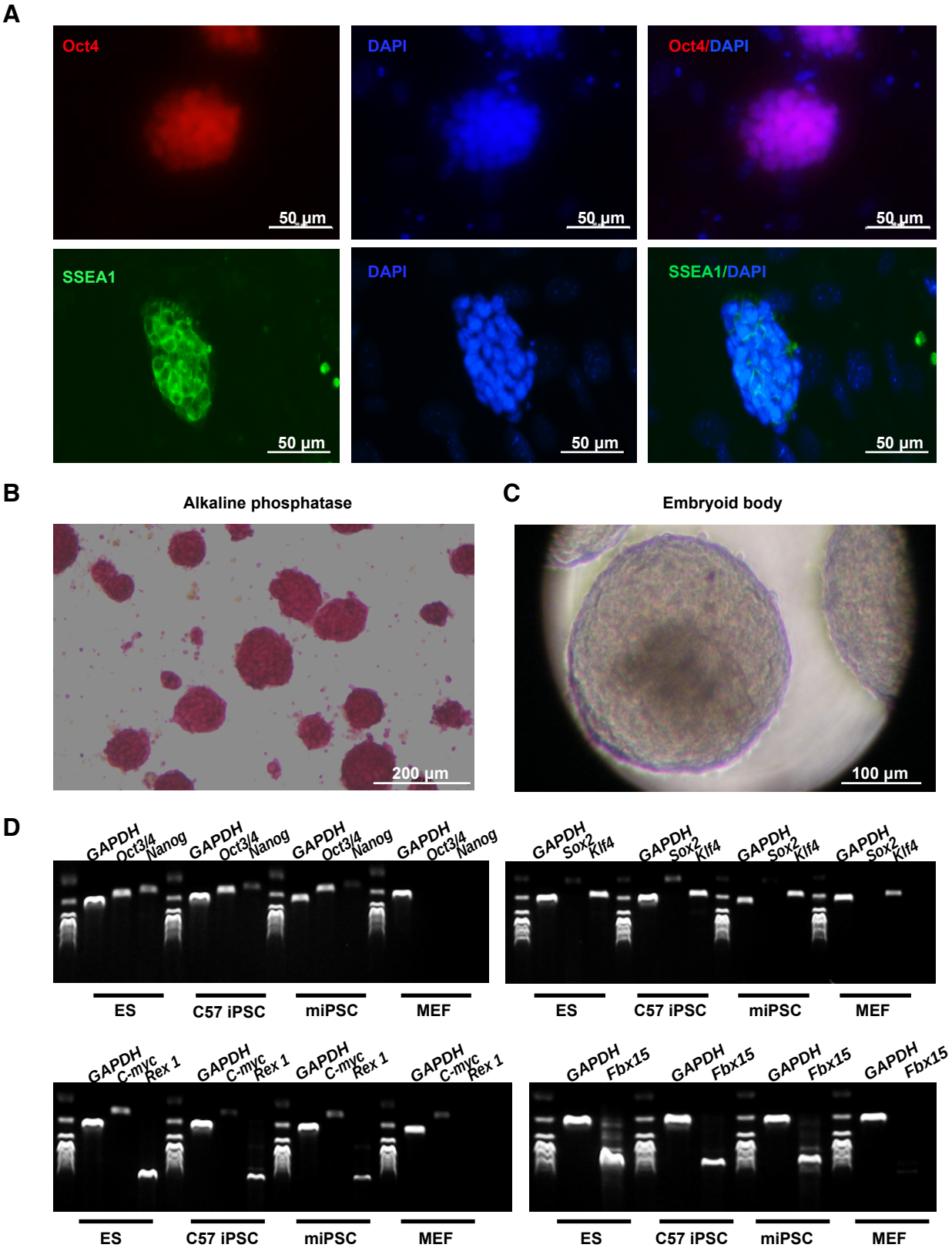
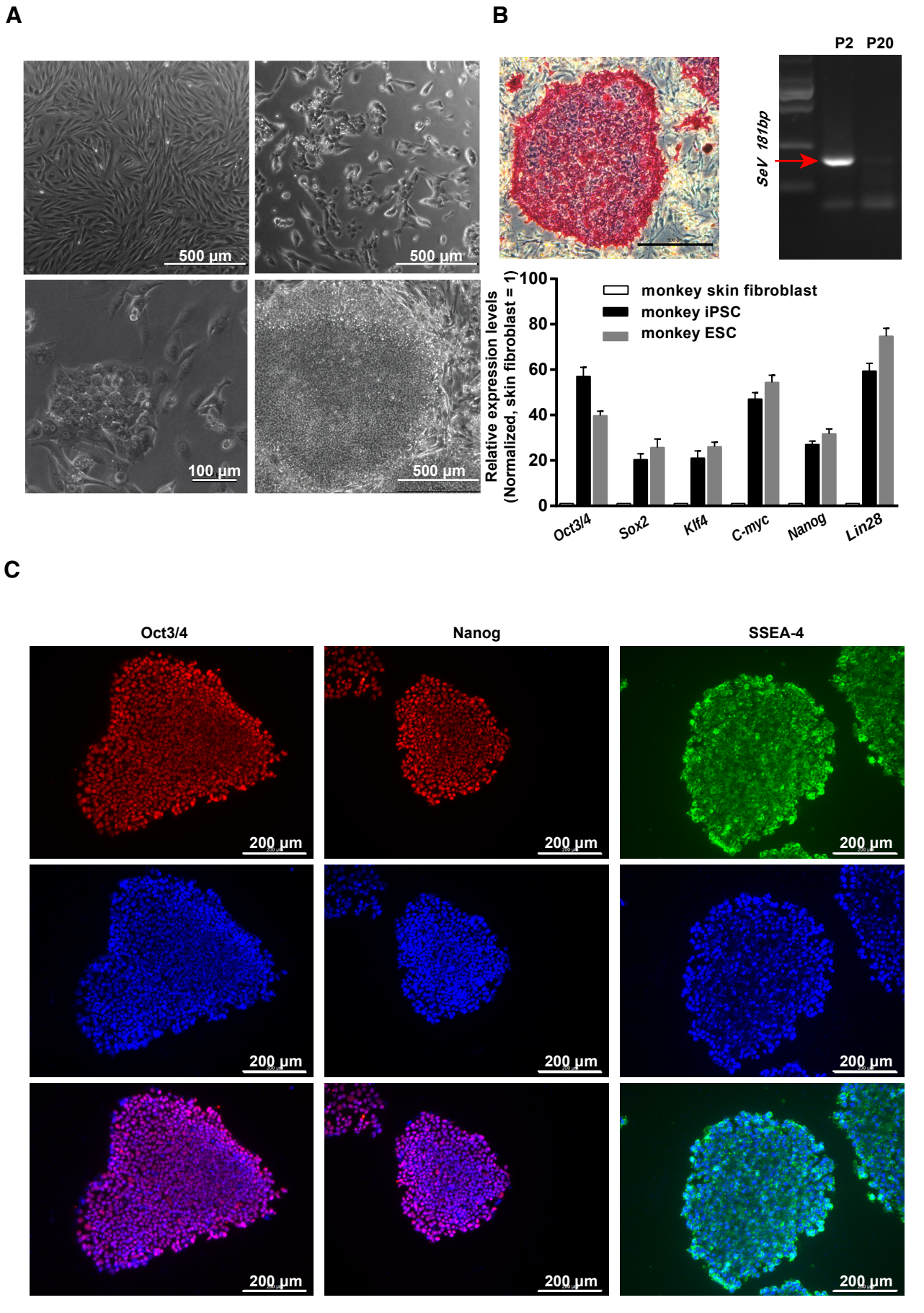


Figure S2. Mouse iPSC identification. (A) Expression of pluripotency markers in iPSCs. The cells were immu-nostained using specific antibodies for Oct4 and SSEA-1. Images were acquired using a fluorescence micro-scope. All iPSCs were strongly positive for both Oct4 and SSEA-1. (B) The cells possessed strong alkaline phosphatase activity. (C) The cells formed embryoid bodies when cultured in the absence of leukemia inhibitory factor. (D) The cells expressed pluripotency markers in a manner similar to embryonic stem cells.


A
500 μm
500 μm
100 μm
500 μm
B
P2 P20
SeV 181bp
monkey skin fibroblast
monkey iPSC
monkey ESC
Relative expression levels
(Normalized, skin fibroblast = 1)
100
80
60
40
20
0
Oct3/4
Sox2
Klf4
C-myc
Nanog
Lin28
C
Oct3/4
Nanog
SSEA-4
200 μm

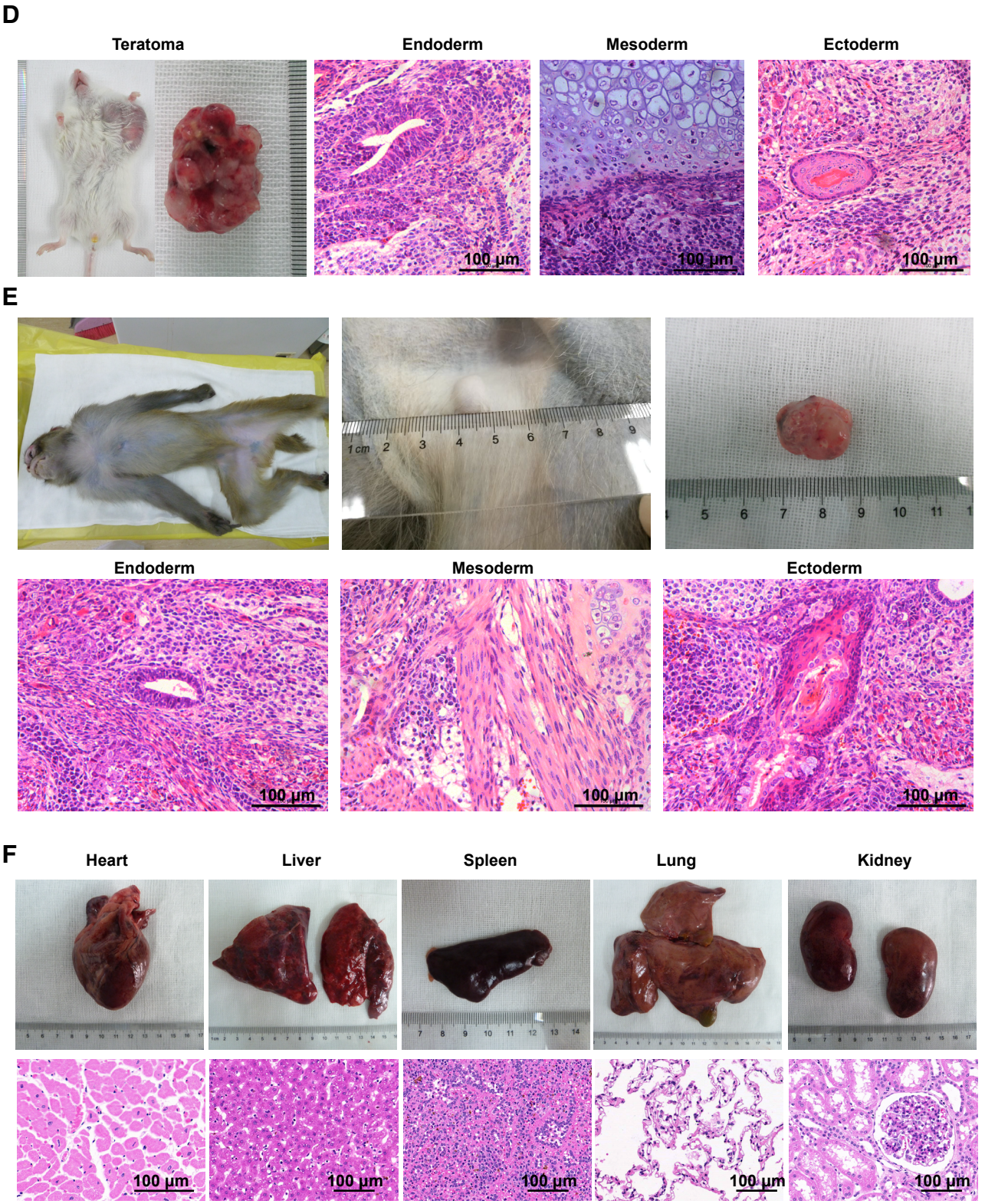
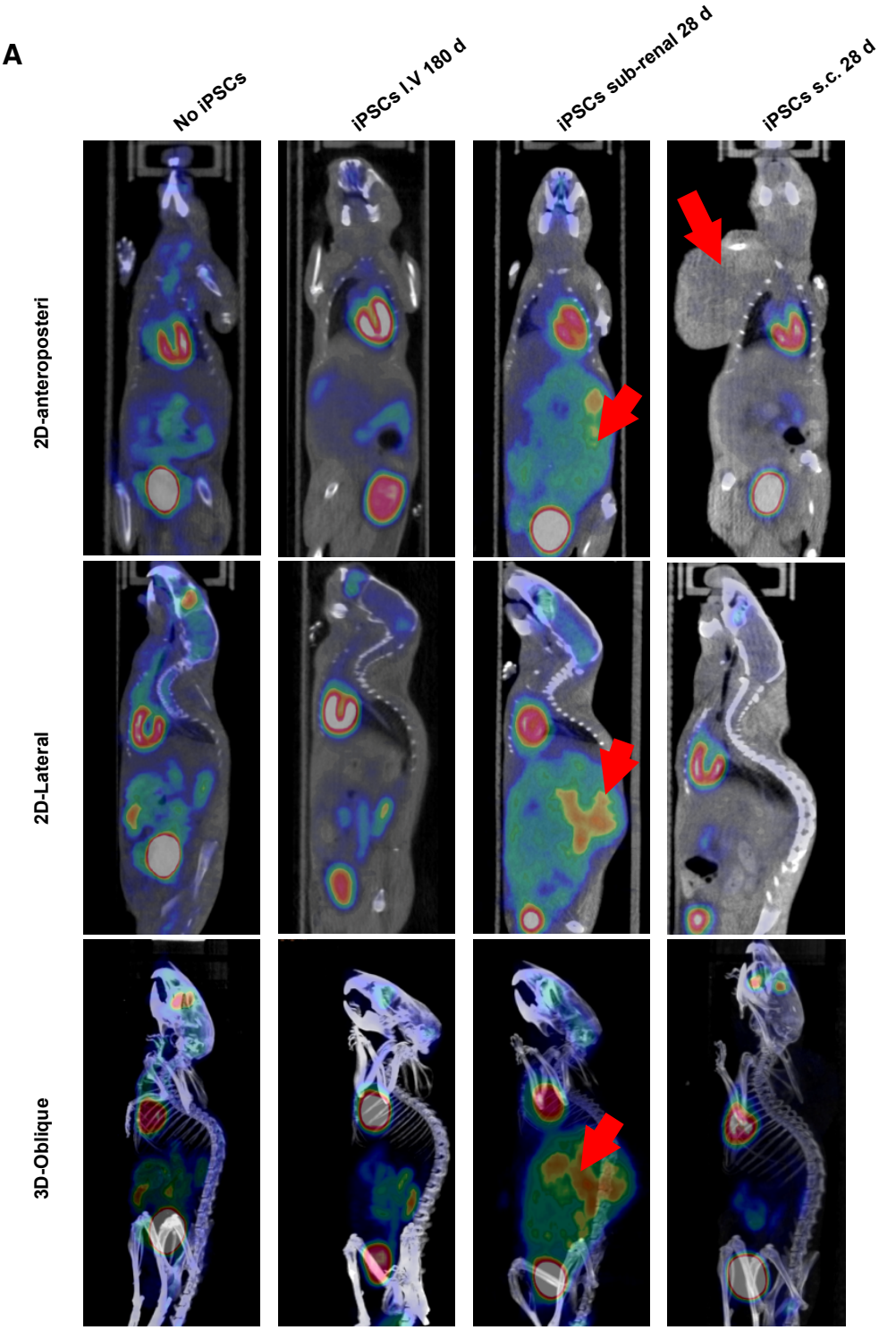


Figure S3. Monkey iPSC identification. (A) Cell morphology during induction. (B) The cells possessed strong alkaline phosphataseactivity(left), and expression of pluripotency markers (middle) and marker of Sendai viral vector disappeared in iPSCs of 20th passage (right). (C) The cells were positively immunostained using specific antibodies for Oct3/4, Nanog, and SSEA-4. Images were acquired using a fluorescence microscope. (D) Histological analyses of teratomas formed in immune-deficient mice. (E) Autologous mon-keys generated from subcutaneously injected iPSCs. The tissues were stained using H&E to identify cells originating from the three germ layers: endocrine glands (endoderm), muscle and cartilage (mesoderm), and epidermis (ectoderm). (F) Tissues outside the injection area of autologous iPSCs had no teratoma.


A
No iPSCs
iPSCs I.V 180 d
iPSCs sub-renal 28 d
iPSCs s.c. 28 d
2D-anteroposteri
2D-Lateral
3D-Oblique

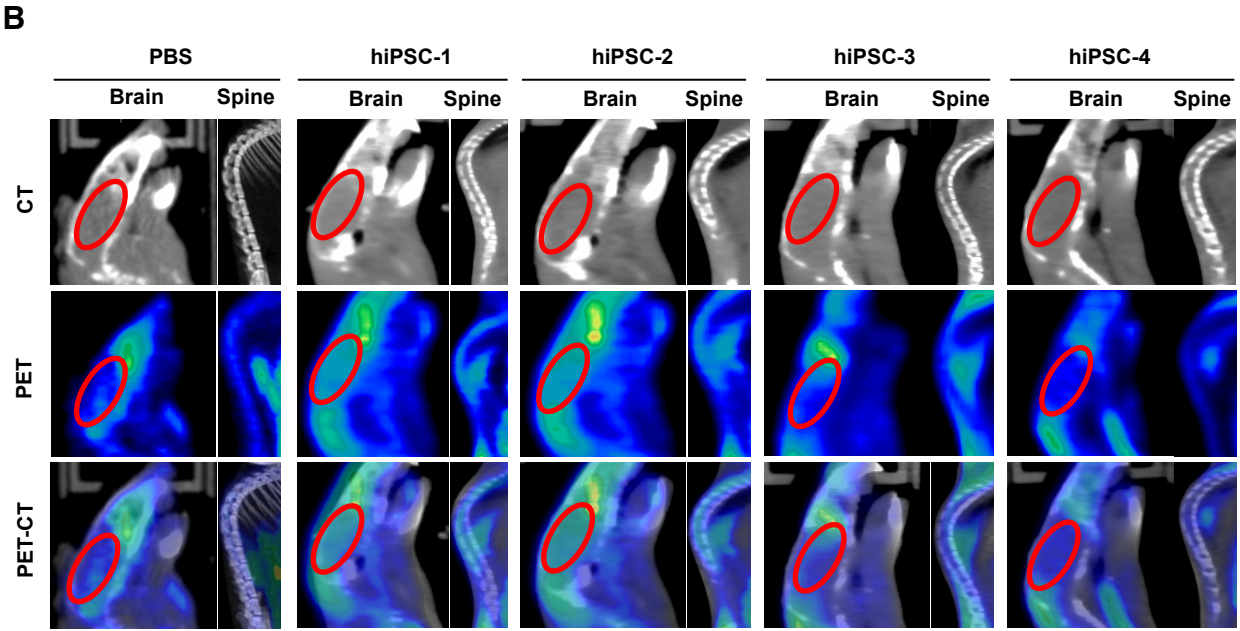


Figure S4. Micro-PET/CT imaging for teratoma detection. (A) 2D images of anteroposterior (top panel) and lateral (middle panel) positions and 3D images of the oblique position (bottom panel) are presented. Representative images of mice receiving no iPSCs, mice 180 days after bolus tail vein injection of 2.5 × 10^8 iPSC/kg body weight, or mice 28 days after receiving 1 × 10^6 iPSC/spot subcutaneously or 1 × 10^6 cells in the intrarenal capsule are shown. Teratomas are indicated by red arrows. (B) Representative brain and spinal cord images of a NOD-SCID mouse without iPSC administration and four NOD-SCID mice receiving iPSC lines from four diabetic foot patients, captured 180 days after a bolus tail vein injection of 2.5 × 10^8 iPSC / kg body weight. No teratoma was detected in the brain and spinal cord.

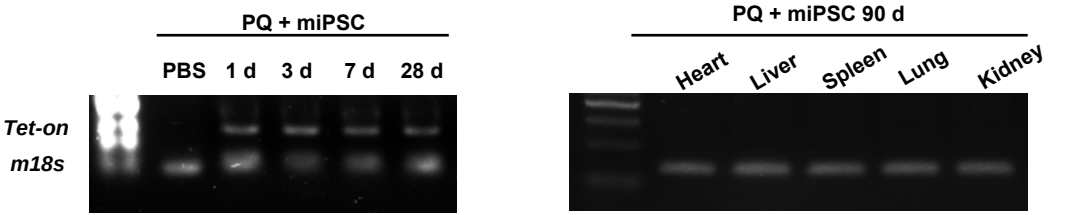


Figure S5. Survival of intravenously injected syngeneic iPSCs in major organs of paraquat-intoxicated mice. (A) PCR product from the *Tet-on* gene isolated from lungs of paraquat-intoxicated mice 1, 3, 7 and 28 days after intravenous iPSC injection.(B) Heart, liver, spleen, lung and kidney of paraquat-intoxicated mice 90 days after intravenous iPSC injection.

Table S1. Key resources table

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Antibodies		
Peroxidase AffiniPure Donkey anti-Rat IgG (H+L) (used at 1:5000)	Jackson ImmunoResearch Inc	Cat# 712-035-153
Peroxidase AffiniPure Donkey anti-Mouse IgG (H+L) (used at 1:5000)	Jackson ImmunoResearch Inc	Cat# 715-035-151
AffiniPure Fab Fragment Donkey anti-Mouse IgG(H+L) (used at 1:5000)	Jackson ImmunoResearch Inc	Cat# 715-007-003
Mouse monoclonal anti-Oct3/4 antibody (used at 1:200)	Santa Cruz Biotechnology	Cat# sc-101534
Mouse monoclonal anti-SSEA1 (MC480) antibody (used at 1:100)	Cellular Signaling Technology	Cat# 4744
Rabbit polyclonal anti-Nanog antibody (used at 1:100)	abcam	Cat# ab80892
Rabbit polyclonal anti-Sox2 antibody (used at 1:100)	abcam	Cat# ab97959
Mouse monoclonal anti-Tra1-60 antibody (used at 1:100)	abcam	Cat# ab16288
Mouse monoclonal anti-SSEA4 Antibody (used at 1:100)	Thermo Fisher Scientific	Cat# MA1-021
Mouse monoclonal anti-SSEA4 Antibody (used at 1:100)	abcam	Cat#ab16287
Mousemonoclonal antibodySTEM 121	Takara Bio Inc	Cat#Y40410
Bacterial and Virus Strains		
Sendai virus	Thermo Fisher Scientific	Cat# A16518
Chemicals, Peptides, and Recombinant Proteins		
Lipofectamine 2000	Thermo Fisher Scientific	Cat#11668019
Dulbecco’s modified Eagle’s medium	Thermo Fisher Scientific	Cat#11965175
DMEM/F12	Thermo Fisher Scientific	Cat# 10565018
Fetal bovine serum ,FBS	Thermo Fisher Scientific	Cat#10100147
Polybrene	Sigma-Aldrich	Cat#107689-10G
β-mercaptoethanol	Sigma-Aldrich	Cat#97622-10ML
Penicillin-Streptomycin-Glutamine	Thermo Fisher Scientific	Cat#10378016
Doxycycline	Sigma-Aldrich	Cat#D9891-1G
Leukemia inhibitory factor	Millipore	Cat#LIF2005
Ficoll-Paque PREMIUM	GE Healthcare	Cat#17-1440-02
Serum-free medium	Nobimpex	Cat#N101-0500
Knockout serum replacement, KSR	Thermo Fisher Scientific	Cat#10828028
L-glutamine	Thermo Fisher Scientific	Cat#25030081
Non-essential amino acids, NEAA	Thermo Fisher Scientific	Cat#11140050
Basic fibroblast growth factor, bFGF	Thermo Fisher Scientific	Cat#PHG0266

Matrigel	BD Biosciences	Cat#354277
6’-diamidino-2-phenylindole, DAPI	Sigma-Aldrich	Cat#D8417
Donkey serum	Sigma-Aldrich	Cat#D9663
Triton X-100	Sigma-Aldrich	Cat#T9284
Valproic acid	Sigma-Aldrich	Cat#PHR1061
Alkaline phosphatase detection kit	Sigma-Aldrich	Cat#86R-1KT
SYBR Green PCR Master Mix	Thermo Fisher Scientific	Cat#4309155
TRIzol Reagent	Thermo Fisher Scientific	Cat#15596026
SuperScript III	Thermo Fisher Scientific	Cat#18080044
EC growth medium，ECM	ScienCell Research Laboratories	Cat#1001
Mitomycin C	Sigma	Cat#M0503
Paraformaldehyde	Sinopharm chemical reagent Co, Ltd	Cat#30525-89-4
LPS	Sigma-Aldrich	Cat#L2880-10MG
Pentobarbital sodium	Sigma-Aldrich	Cat#P3761
Collagenase IV	Thermo Fisher Scientific	Cat#17104019
Trypsin-EDTA	Thermo Fisher Scientific	Cat#25200056
Streptozotocin	Sigma-Aldrich	Cat#S0130-50MG
Low melting point agarose	Biowest	Cat#111860
Paraquat dichloride hydrate	Sigma-Aldrich	Cat#36541
Carbon Tetrachloride	Sinopharm chemical reagent Co, Ltd	Cat#10006428
Recombinant Anti-human CD3 monoclonal antibody	T&L Biological Technology	Cat# TL-101
Recombinant human Interleukin-2	T&L Biological Technology	Cat# TL-104
Experimental Models: Cell Lines		
293FT	ATCC	ATCC PTA-5077
Experimental Models: Organisms/Strains		
Mouse: C57BL/6	Shanghai Laboratory Animal Co. Ltd	
Mouse: SCID-NOD	Vital River Laboratory Animal Technology Co. Ltd	
Monkey: macaque	Dongwu Experimental Monkey Farm	
Oligonucleotides		
Primer: **Macaque Oct3/4(Genbank:NM_001114955.1)** Forward: CAGATCAGCCACATTGCCCAG Reverse: CAAAAGCCCTGGCACAAACTCT	This paper	N/A

Primer: **Macaque Sox2(Genbank:NM_001142940.1)** Forward: GGTTACCTCTTCCTCCCACTCC Reverse: CCTCCCATTTCCCTCGTTTT	This paper	N/A
Primer: **Macaque Klf4(Genbank:NM_001142793.2)** Forward: TTTTCGGTTTTGGCTTCGTTTC Reverse: GTCCAGGTCCAGGAGATCGTTG	This paper	N/A
Primer: **Macaque c-Myc(Genbank:NM_001142873.1)** Forward GCGTCGTGGGAAGGGAGATAC Reverse: CACCGAGTCGTAGTCGAGGTCAT A	This paper	N/A
Primer: **Macaque Nanog(Genbank:XM_001112791.3)** Forward CCTATGCCTGTGATTTGTGGG Reverse AGGTTGTTTGCCTTTGGGAC	This paper	N/A
Primer: **Macaque Lin28(ENSMMUG00000044953)** Forward: GTTCGGCTTCCTGTCCAT Reverse: CACTCCCAATACAGAACACCC	This paper	N/A
Primer: **Macaque GAPDH(Genbank:NM_001195426.1)** Forward: GGTGTGAACCATGAGAAGTATGA Reverse: GAGTCCTTCCACGATACCAAAG	This paper	N/A

Primer: Tet-On Forward: AGCACAACTACGCCGCACCC Tet-On Reverse: TGCACCAGAGTTTCGAAGC-	This paper	N/A
Primer: **human Oct3/4(Genbank:NM_001173531.2)** Forward: CGAGAAGGATGTGGTCCGAG Reverse: GAGACAGGGGGAAAGGCTTC	This paper	N/A
Primer: **human Sox2(Genbank:NM_003106.3)** Forward: CCCCTGTGGTTACCTCTTCC Reverse: CCTCCCATTTCCCTCGTTTT	This paper	N/A
Primer: **human Klf4(Genbank:NM_001314052.1)** Forward: CCGCTCCATTACCAAGAGC Reverse: TTTCTCACCTGTGTGGGTTC	This paper	N/A
Primer: **human c-Myc(Genbank:NM_001354870.1)** Forward CAGCGACTCTGAGGAGGAAC Reverse: GCTGGTGCATTTTCGGTTGT	This paper	N/A
Primer: **human Nanog (Genbank:NM_001297698.1)** Forward CAATGGTGTGACGCAGAAGG Reverse TGCACCAGGTCTGAGTGTTC	This paper	N/A

Primer: **human GAPDH(Genbank:NM_001256799.2)** Forward: GATTCCACCCATGGCAAATTC Reverse: CTGGAAGATGGTGATGGGATT	This paper	N/A
Primer: **mouse Oct3/4(Genbank:NM_001252452.1)** Forward: GCATACGAGTTCTGCGGAGG Reverse: TCTCCAACTTCACGGCATTG	This paper	N/A
Primer: **mouse Sox2(Genbank:NM_011443.4)** Forward: CAGGAGAACCCCAAGATG Reverse: GTGTACTTATCCTTCTTC	This paper	N/A
Primer: **mouse Klf4(Genbank:NM_010637.3)** Forward: GCAGTCACAAGTCCCCTCTC Reverse: CTGTGTGAGTTCGCAGGTGT	This paper	N/A
Primer: **mouse c-Myc(Genbank:NM_001177352.1)** Forward CAACGTCTTGGAACGTCAGA Reverse: CTCGTCTGCTTGAATGGACA	This paper	N/A
Primer: **mouse Nanog (Genbank:NM_001289828.1)** Forward GGAACGCCTCATCAATGC Reverse TTTGTTTGGGACTGGTAGAAG	This paper	N/A

Primer: **mouse** **Rex1(Genbank:NM_025852.3)** Forward GCCAGCAGCTCCTGCACACA Reverse TGAGCTCGCCCCAACCCTCA	This paper	N/A
Primer: **mouse** **Fbx15(Genbank:NM_015798.4)** Forward GGTGGGGCTGTGGCAGGAGA Reverse AGAGTAAGCCGGCTGCGGGA	This paper	N/A
Primer: **mouse** **GAPDH(Genbank:NM_001289726.1)** Forward CTCATGACCACAGTCCATGC Reverse TTCAGCTCTGGGATGACCTT	This paper	N/A
Recombinant DNA		
FUW-OSKM	Addgene	Cat #20328
psPAX2	Addgene	Cat #12260
pMD2.G	addgene	Cat #12259
Other		
4-mm biopunch	FRAY	CE0413
0.015-inch-diameter Straight Fixed Core Wire Guide C-SF-15-156	Cook	Cat#G02426