Supplementary materials
Figures and Legends

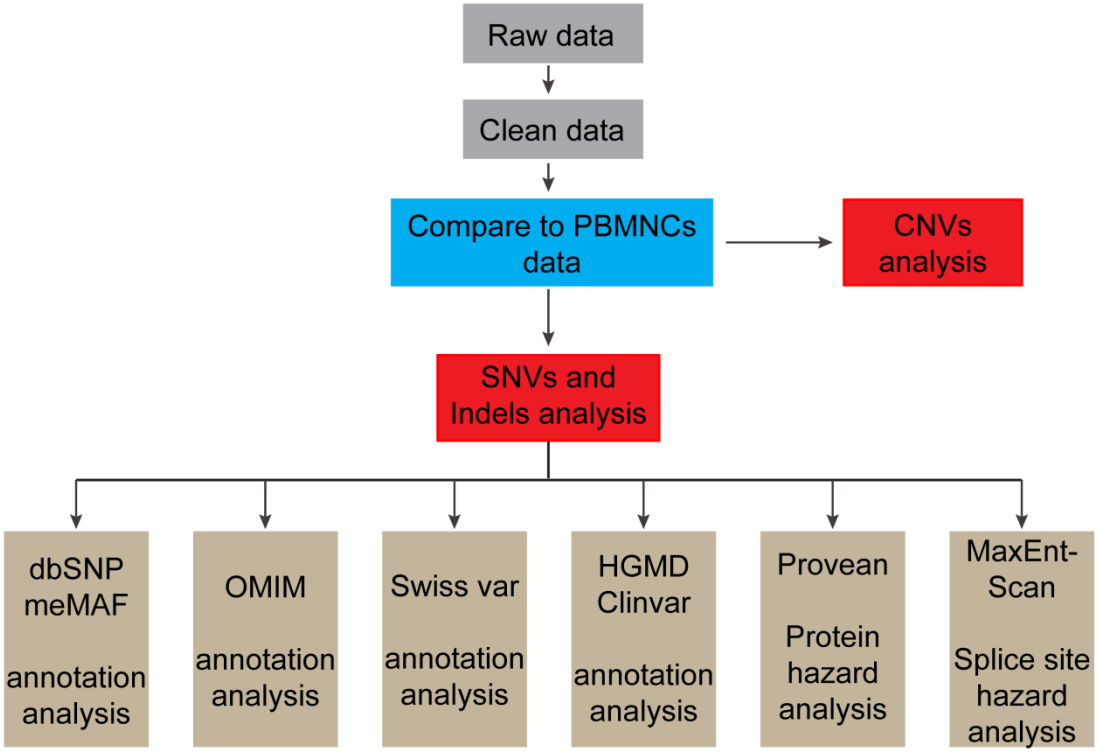

Figure S1. Flow diagram of whole-genome sequencing data analysis.

The raw data of genomic DNA sequencing were acquired by using illunima Hiseq, and then the raw data were compared with hg19 database to generate the clean data. The data from the daughter iNSCs were compared with those from the parental PBMNCs to obtain the variants between them. At last, the SNVs, Indels and CNVs were systematically analyzed by referring to relevant databases and by using different software tools.

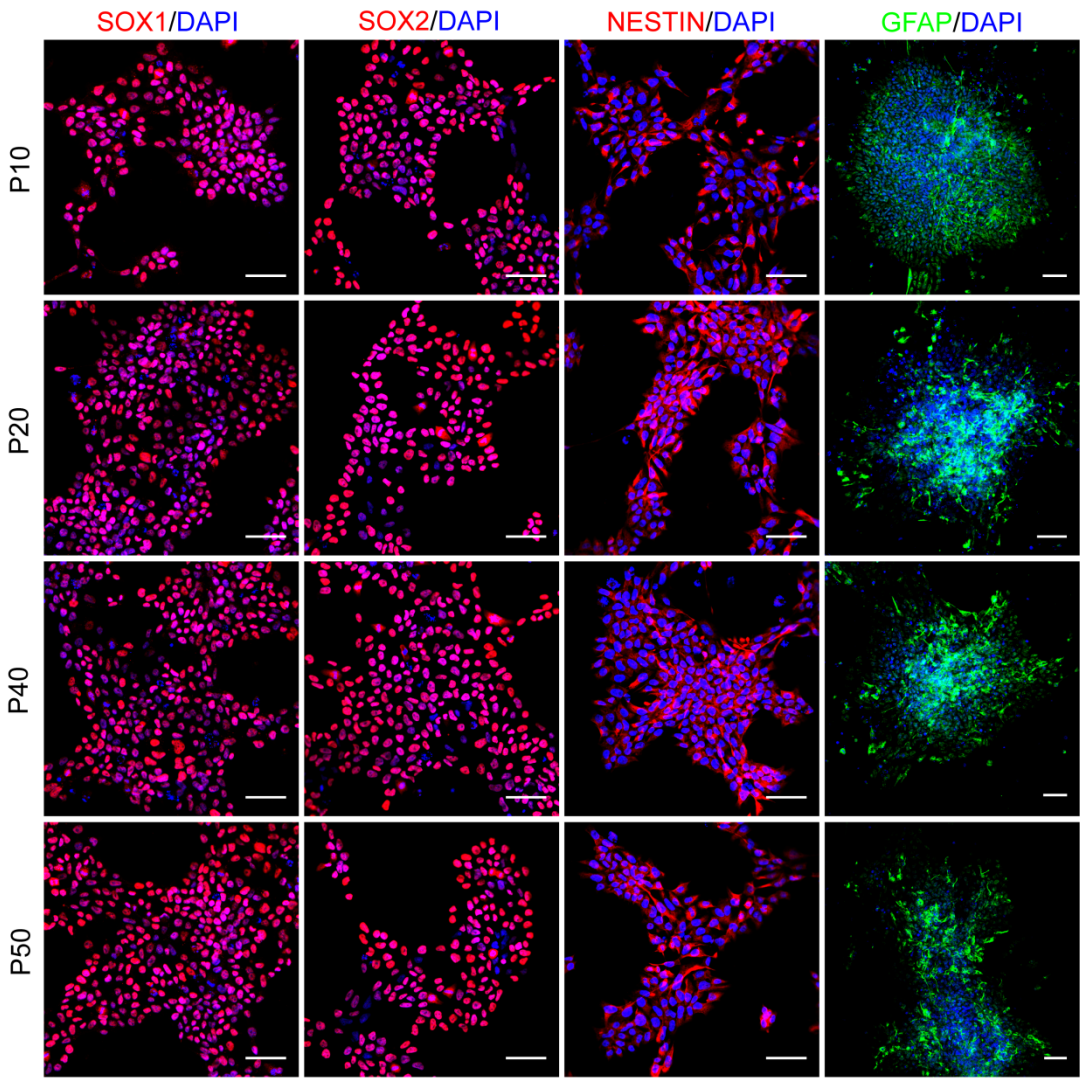

Figure S2. Characterization of iNSCs of various passage numbers.

iNSCs of P10, P20, P40, and P50 all stained positive for SOX1, SOX2, NESTIN and GFAP, as did iNSCs of P30, which was shown in Figure 2.

P10, passage No. 10; Scale bars, 50 μm.

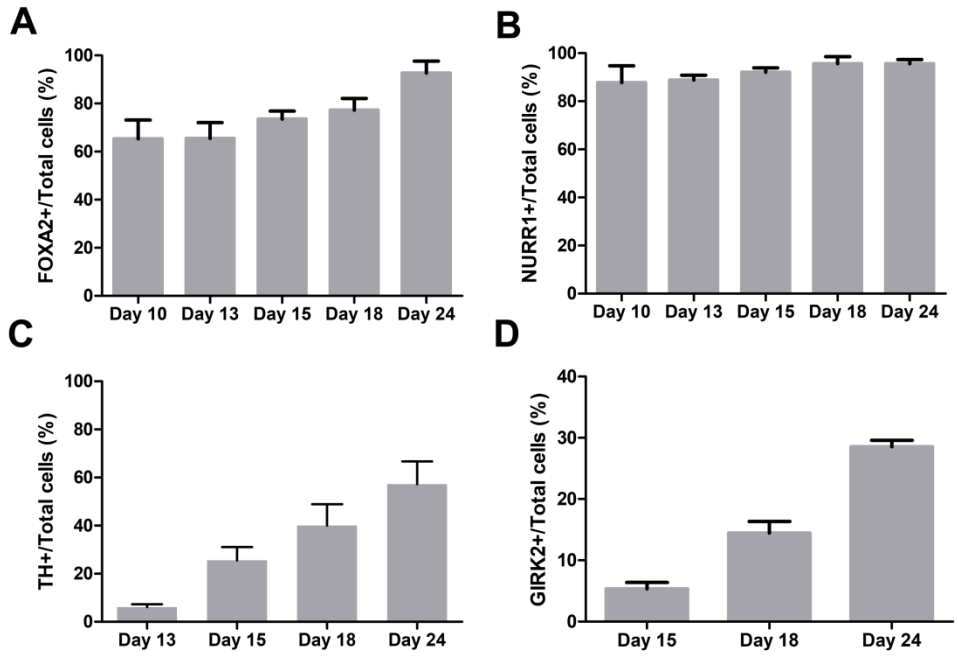

Figure S3. Differentiation of iNSCs into midbrain dopamine neurons *in vitro*.

(A) The percentages of FOXA2+ cells at different differentiation time points. The values represented mean ± SEM in all the figures (n=3).

(B) The percentages of NURR1+ cells at different differentiation time points (n=3).

(C) The percentages of TH+ cells (n=3).

(D) The percentages of GIRK2+ cells (n=3).

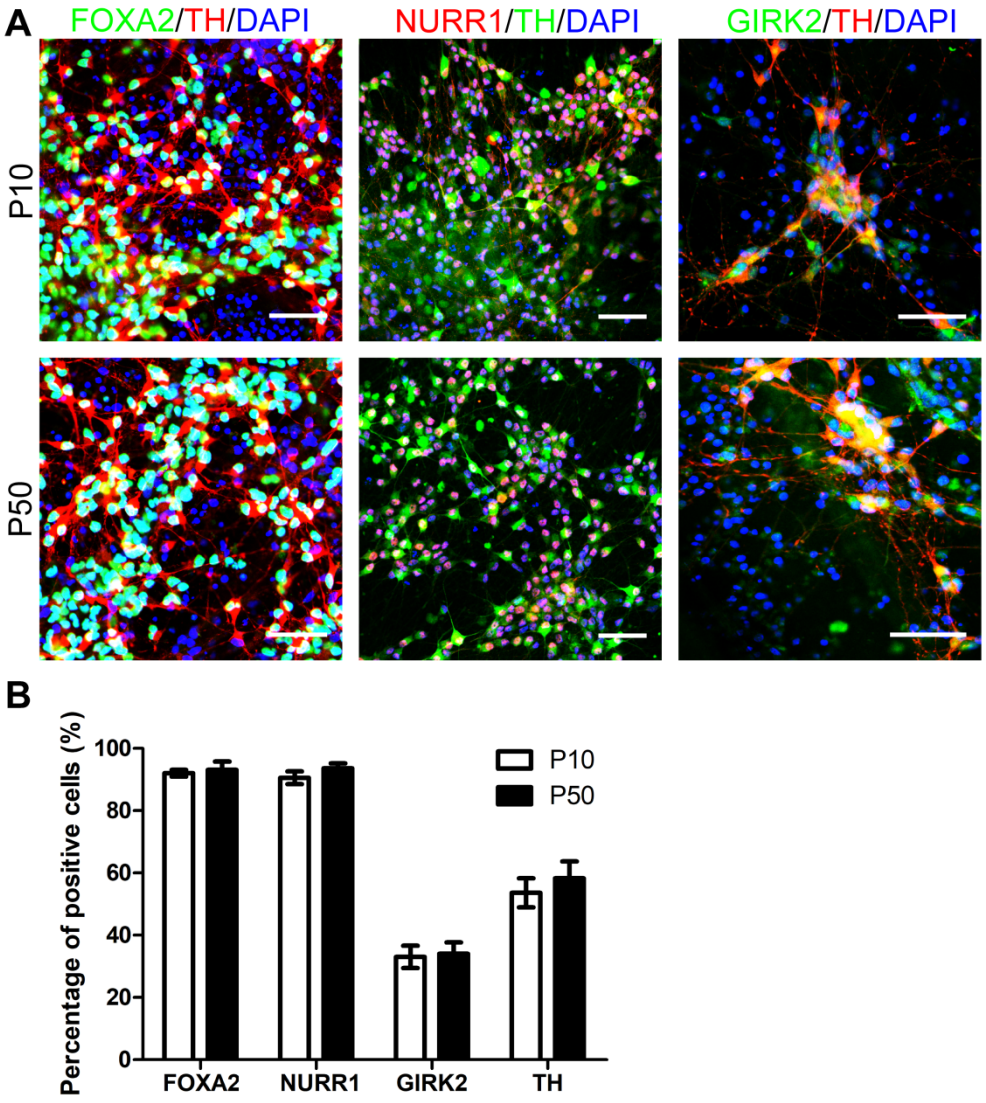

Figure S4. Differentiation to DA neurons from iNSCs of early and late passages.

(A) Representative pictures of mDA neurons positive for FOXA2, NURR1, GIRK2, and TH, which were differentiated for 24 days from iNSCs of P10 and P50.

(B) The percentages of FOXA2-, NURR1-, GIRK2-, and TH-positive cells were comparable as differentiated from iNSCs of P10 vs. P50.

P10, passage No. 10; Scale bars, 50 μm.

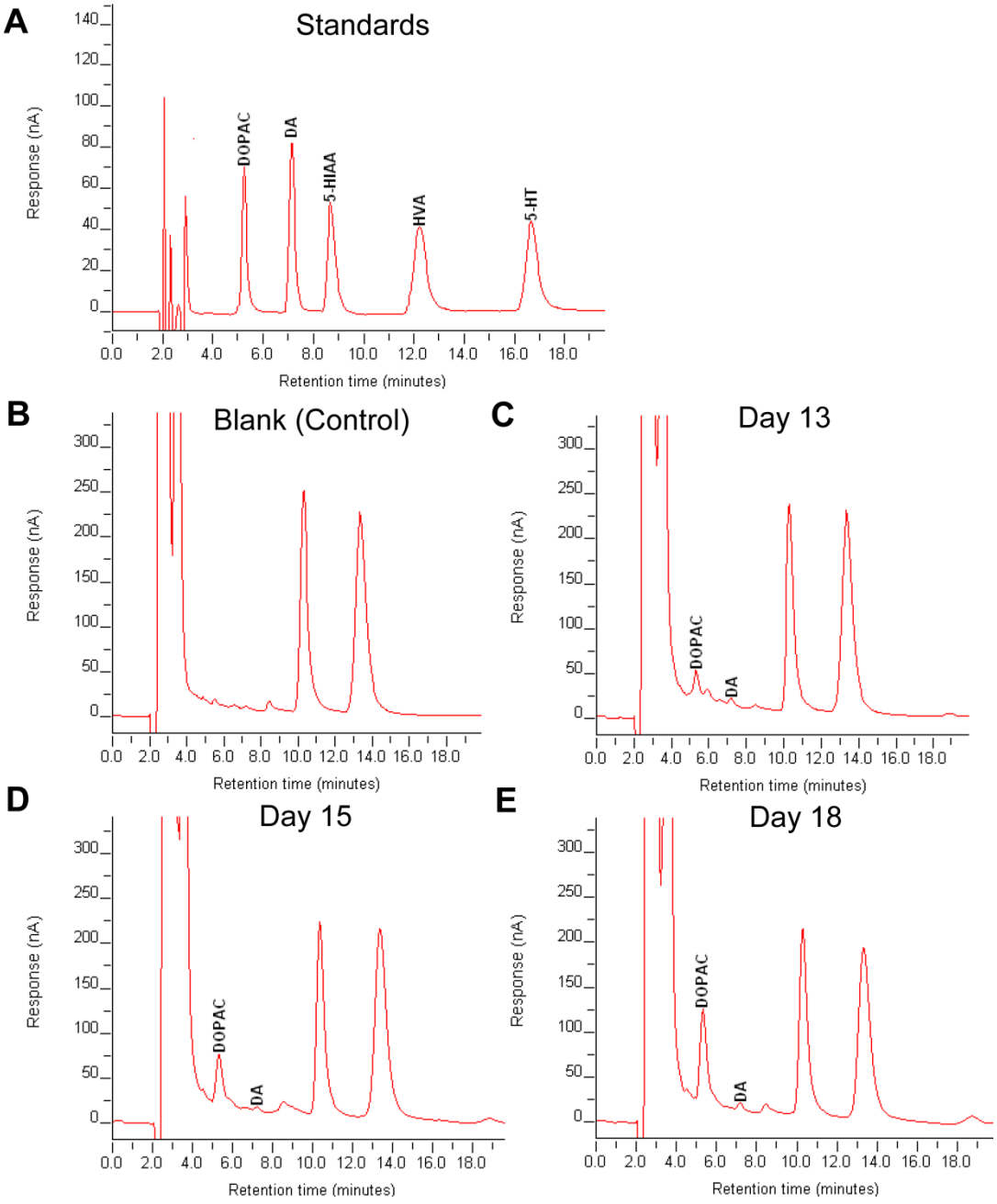

Figure S5. HPLC analysis at different time points.

(A) HPLC curve for DA, DOPAC, HVA, 5-HIAA, and 5-HT standards. DA, dopamine; DOPAC, 3,4-dihydroxyphenylacetic acid; HVA, homovanillic acid; 5-HIAA, 5-Hydroxyindoleacetic Acid; 5-HT, 5-hydroxytryptamine.

(B) HPLC curve for blank control (n=3).

(C) HPLC curve for DA, DOPAC on differentiation day13 (n=6).

(D) HPLC curve for DA, DOPAC on differentiation day15 (n=6).

(E) HPLC curve for DA, DOPAC on differentiation day18 (n=6).

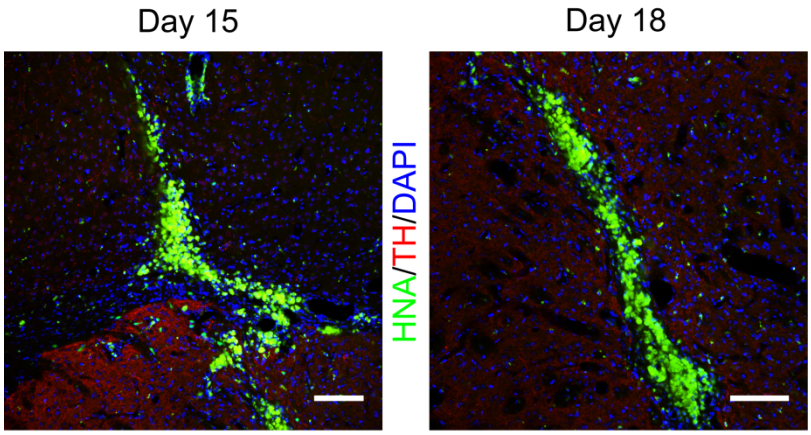

Figure S6. Immunostaining on cells of differentiation day 15 and day 18 that had been transplanted into naïve SCID-beige mice.

Immunofluorescent staining for TH (red) and HNA (green) on differentiation day 15 and day 18 groups in SCID-beige mice. Dead cells were auto-fluorescent and showed colors in all three channels. HNA, human nuclei antibody. Scale bars, 100 μm.

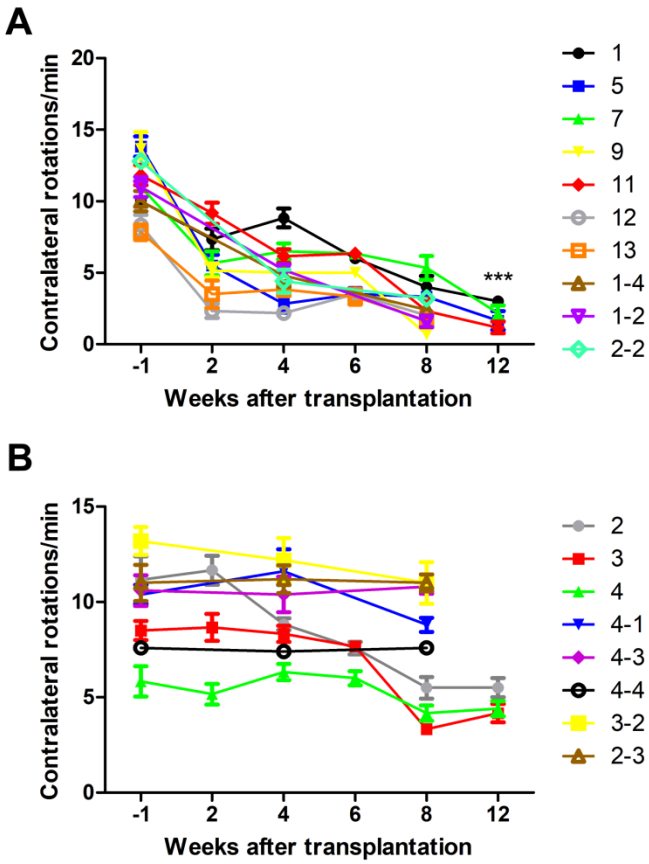

Figure S7. Apomorphine-induced contralateral rotations from each individual SCID-beige PD mouse.

(A) The results of apomorphine-induced contralateral rotations from individual SCID-beige mouse in "6-OHDA+cells" group. ***$p < 0.001$ by two-way ANOVA with Dunnett's multiple comparison test.

(B) The results of apomorphine-induced contralateral rotations from individual SCID-beige mouse in "6-OHDA+buffer" group.

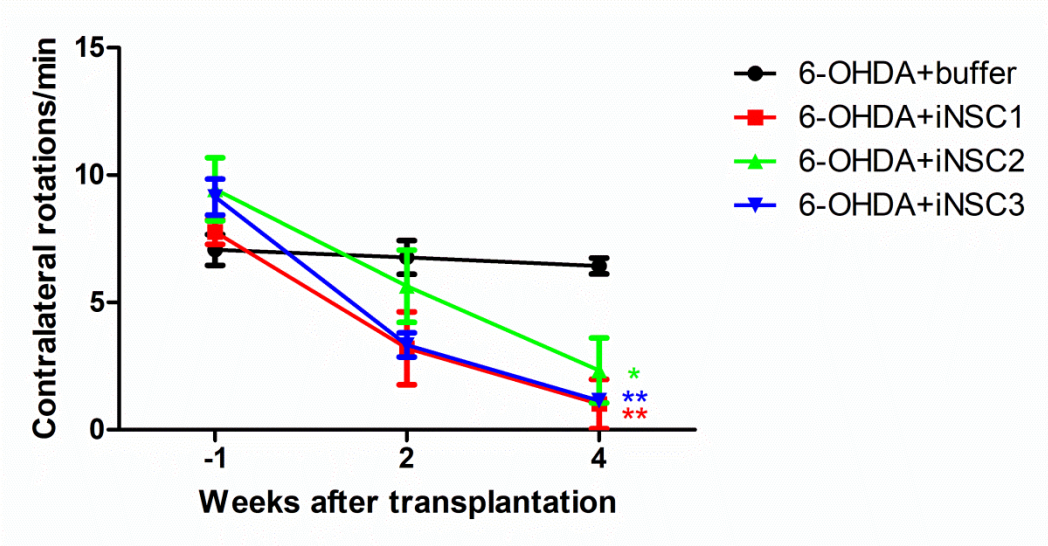

Figure S8. Apomorphine-induced contralateral rotations in C57BL/6 PD mice.

The results of apomorphine-induced contralateral rotations in "6-OHDA+buffer", "6-OHDA+iNSC1", "6-OHDA+iNSC2" and "6-OHDA+iNSC3" C57BL/6 mouse groups. *$p < 0.05$; **$p < 0.01$ by two-way ANOVA with Dunnett's multiple comparison test.

Supplementary Tables

Table S1. Primer sequences and product length of target genes.

Genes	Forward (5’-3’)	Reverse (5’-3’)	Product length (bp)
OCT4(exo)	AGTGAGAGGCAACCTGGAGA	AGGAACTGCTTCCTTCACGA	658
SOX2(exo)	TGGCTCTCCTCAAGCGTATT	AGGAACTGCTTCCTTCACGA	498
KLF4(exo)	TGGCTCTCCTCAAGCGTATT	GTGGAGAAAGATGGGAGCAG	253
c-MYC(exo)	GCGTCCTGGGAAGGGAGATCCGGAGC	TTGAGGGGCATCGTCGCGGGAGGCTG	328
SEV	GGATCACTAGGTGATATCGAGC	ACCAGACAAGAGTTTAAGAGATATGTATC	152
HES5	GCGACCGCATCAACAGCA	GCGTGGAGCGTCAGGAACT	235
SOX1	GTTTTTTGTAGTTGTTACCGC	GCATTTACAAGAAATAATAC	173
SOX2	AGTCTCCAAGCGACGAAAAA	TTTCACGTTTGCAACTGTCC	189
FABP7	TGTGACCAAACCAACGGTAAT	CTTTGCCATCCCATTTCTGTA	200
PAX6	GGTGAGAAGTGTGGGAACCG	GTGCTGCTGTTGTTGCTTGA	183
GAPDH	GTGGACCTGACCTGCCGTCT	GGAGGAGTGGGTGTCGCTGT	153
ESRP1	TAGGTTGACAGGGTGGAAT	GCACTGGCTATCAAAGGAG	428
CCDC87	TTTTCAATGGCTTTGGGATC	GGAGGCTGGCAGATGAGTT	484
KLF4	CTCAGCACTTCCTCAAGACCCAG	TCCGACGGCTCCCTTCAACC	438
CACNA1A	TTCTGTCGGACGGGGATG	GGGTGGACTGGGGATTGC	586
YARS	ATAATATCCACAGGCAACAA	TACCTAAAGGAGGCAAAGC	531
POU5F1B	CCGCCGTATGAGTTATGTG	CTCGGTTCTCGATACTGGTT	529
GOLGA6L2	GGGGAGGTGATTGGACTTA	GCGGGAGATAGAGGTGAGTG	418
ATP9B	GTTGTTGCTGGTCTCCCG	TCTGGCTAGGTTGACTTAGGAG	410
SCNN1D	CATGTCTCCGCTCCATCC	CCCCACCCCACCACTTT	499
PSME4	GCTGAGACTCCCACTAAC	GTAATGGAAAATTATGTGCT	533
HHATL	TTGAAGACAGGTGGAAAGTG	CGAGTGGGTGATGTGGTT	543
PCDHA12	GTCATTGCCCTGATTAGCGT	TCCAGCTCCTCGTGGTCTAG	485
RSPH4A	TCGCTGTAATTGGTTCAA	TTCACTCCCTATCATCCC	292
OR1L8	CAATAGCCTTGTCTCACAT	CTCACCTCCACTCACTCC	600
TNN	AGGATCTATCTGCCAATCT	GTACAACCAGCAATGTGAT	573

Note: exo means transgenes from Sendai virus.

Table S2. Verification of SNVs by PCR and Sanger sequencing.

Sample	Gene	SNV site	SNV detected by WGS	SNV by PCR and sequencing	Correct /False
Epi iNSC	ESRP1	95690440	C＞A	C＞A	Correct
Epi iNSC	CCDC87	66359313	G＞A	G＞A	Correct
Epi iNSC	KLF4	110249842	A＞C	A＞C	Correct
Epi iNSC	CACNA1A	13617016	T＞A	T＞A	Correct
Epi iNSC	YARS	33246663	A＞T	A＞T	Correct
Epi iNSC	POU5F1B	128428514	A＞G	A＞G	Correct
Sev iNSC1	GOLGA6L2	23689091	G＞A	G＞A	Correct
Sev iNSC1	ATP9B	77089291	G＞A	G＞A	Correct
Sev iNSC1	SCNN1D	1225717	C＞T	C＞T	Correct
Sev iNSC1	PSME4	54159183	C＞T	G＞G	False
Sev iNSC1	HHATL	42740301	G＞A	G＞A	Correct
Sev iNSC2	SCNN1D	1225717	C＞T	C＞T	Correct
Sev iNSC2	PCDHA12	140256370	C＞T	C＞T	Correct
Sev iNSC2	RSPH4A	116950826	G＞C	G＞C	Correct
Sev iNSC2	OR1L8	125330074	A＞G	A＞G	Correct
Sev iNSC2	TNN	175096104	C＞A	C＞C	False

Note: Epi iNSC, Episomal iNSC.

Table S3. Summary of SNVs and Indels under different screening conditions.

Condition	Cell lines	SNVs (genes)	Indels (genes)
Parental VAF=0 reads≥35 iNSC lines VAF≥0.4	Episomal-iNSC	28 (19)	3 (3)
	Sev-iNSC1	27 (27)	1 (1)
	Sev-iNSC2	13 (13)	0 (0)
Common mutation shared by three cell lines		0 (0)	0 (0)
Parental VAF>0 reads≥35 mutation rate ≥0.4	Episomal-iNSC	1 (1)	0 (0)
	Sev-iNSC1	0 (0)	0 (0)
	Sev-iNSC2	0 (0)	0 (0)
Common mutation shared by three cell lines		0 (0)	0 (0)
Parental VAF=0 reads≥35 iNSC lines VAF＜0.4	Episomal-iNSC	32 (19)	1 (1)
	Sev-iNSC1	21 (19)	9 (4)
	Sev-iNSC2	39 (18)	0 (0)
Common mutation shared by three cell lines		(2)	0 (0)
Parental VAF>0 reads≥35 mutation rate ＜0.4	Episomal-iNSC	336 (104)	38 (17)
	Sev-iNSC1	283 (108)	28 (14)
	Sev-iNSC2	332 (118)	70 (22)
Common mutation shared by three cell lines		(64)	(5)

Table S4. Primary antibody sources and dilutions.

Primary antibody	Host	Dilution	Vendor
TH	sheep	1:500	Millipore
TH	rabbit	1:500	Millipore
SOX1	goat	1:500	Santa cruz
SOX2	goat	1:1000	Santa cruz
NESTIN	mouse	1:500	BD bioscience
PAX6	rabbit	1:400	Biolegend
GFAP	rabbit	1:500	Dako
KI67	rabbit	1:500	Millipore
OCT4	mouse	1:200	Santa cruz
OCT4	rabbit	1:500	GeneTex
Sev	rabbit	1:500	MDL
TUJ-1	mouse	1:500	Millipore
TUJ-1	rabbit	1:500	abcam
HNA	mouse	1:500	Millipore
NURR1	rabbit	1:200	Santa cruz
GIRK2	goat	1:400	abcam
FOXA2	goat	1:100	R&D
O1	mouse	1:300	ebioscience
NEUN	rabbit	1:400	Millipore
MAP2	mouse	1:200	Sigma
OLIG2	rabbit	1:500	Millipore
ASCL1	mouse	1:100	R&D
DCX	goat	1:200	Santa cruz
SYNAPSIN	mouse	1:500	Millipore