SUPPLEMENTARY DATA

Supplementary Table 1. Human iPSCs

hiPSC#1	Commercial foreskin fibroblasts (CRL-2522, ATCC, Manassas, VA, USA)	Newborn, M	Lentiviral transduction	OCT4, SOX2, cMYC and KLF4
hiPSC#2	Dermal fibroblasts	45y, M	Retroviral transduction	OCT4, SOX2, cMYC and KLF4
hIPSC#3	Commercial dermal fibroblasts (C-013-5C, Life Technologies)	Adult, F	Episomal transduction	OCT4, SOX2, cMYC and KLF4

hiPSCs submitted to mechanical passage were seeded on Matrigel (Corning), and cultured in mTESR1 (StemCell Technologies).

SUPPLEMENTARY DATA

Supplementary Table 2. Antibodies

Antibody	Reference	Species	IF	FACS	WB	IHC
Anti-human cytoplasm	StemCells Incorporation STEM121	Mouse				1/1000
anti-human mitochondria	MAB1273 – Millipore	Mouse				1/100
AKT	Santa Cruz H136	Rabbit			1/500	
C/EBPα	Santa Cruz 14A4	Rabbit	1/100		1/250	
Caveolin1	BD Biosciences 610059	Rabbit			1/1000	
CD166	BD Biosciences PE 55559263	Mouse		8µL / 100000 cells		
CD29	BD Biosciences APC 561858	Mouse	1/50			
CD29	BD Biosciences PE 555443	Mouse	1/50	8µL / 100000 cells		
CD44	BD Biosciences APC 561858	Mouse	1/50			
CD44	BD Biosciences PE 550989	Mouse	1/50	8µL / 100000 cells		
CD73	BD Biosciences PE 550257	Mouse		8µL / 100000 cells		
Cited1	Cell signaling 5H6	Mouse	1/200			1/100
DIO2	Novus biological NBP1-00178	Goat				1/500
GLUT4	Santa Cruz H61	Rabbit	1/100		1/2500	
Irβ	Santa Cruz 29B4	Mouse			1/600	
Ki67	AbCam Ab 15580	Rabbit	1/200			
Nanog	Cell Signaling D73G4	Rabbit	1/200			
Oct 3/4	3576 – Biovision	Rabbit	1/200			
P-AKT	Santa Cruz Ser473	Rabbit			1/500	
P-PY	Santa Cruz PY99	Mouse			1/2000	
PDGFRα	Cell signaling D1E1E	Rabbit	1/200			
Perilipin1	Progen GP29	Guinea Pig			1/500	1/500
PPARγ	Santa Cruz 7273	Mouse			1/800	
PRDM16	Abcam 106410	Rabbit	1/200		1/1000	1/400
Sox2	AB5603 – Millipore	Rabbit	1/200			
SSEA-3/4	MAB1435 – Millipore	Mouse	1/100			
T Box	R&D systems	Goat	1/100			
Tra-1-60	MAB4360 – Millipore	Mouse	1/100			
Tra-1-81	MAB4381 – Millipore	Mouse	1/100			
UCP1	Abcam 10983	Rabbit	1/400			
UCP1	Abcam 23841	Rabbit			1/1000	1/150
βActin	Sigma A5441	Mouse			1/10000	

FACS: fluorescence-activated cell sorting (for characterization of hiPSC-derived MSCs at passage 6)

For **immunofluorescence microscopy (IF)**, cells were fixed in 3.2% PFA for 15 min at room temperature. Blocking used PBS-BSA 3% 0.1 % Triton X100 or saponin. Primary antibodies were diluted in PBS, 0.01 % Triton X100 or saponin, 3% BSA. Secondary antibodies coupled to Alexa 488 were diluted to 1/1000 in PBS, 0.01% triton X100 or saponin, 3% BSA. Adipocytes were incubated for 15 min in 25 ng/mL Nile Red (#N-1142, Life Technologies) or Bodipy$^{493/503}$ (#D3922, Life Technologies). Cells were incubated for 5 min in DRAQ5 (#4084, Cell Signaling Technology) before mounting (Fluoromount-G, Southern Biotech). Cells preparations were observed with a confocal microscope (Leica SP2).
For **Western Blot (WB),** samples were lysed in 50 mM Tris, pH 7.4, 270 mM sucrose, 1 mM Na–orthovanadate, pH 10, 1 mM EDTA, 1 mM EGTA, 10 mM Na-β-glycerophosphate, 50 mM NaF, 5 mM Na-pyrophosphate, 1% (w/v) Triton X-100, 0.1% (v/v) 2ß-mercaptoethanol, and Complete protease inhibitors (Roche), centrifuged (15,000*g*, 4°C for 10 min) and stored at −20°C. Protein concentrations were determined by Biorad protein assay kit. Samples were subjected to SDS/PAGE, blotted and protein signals were visualized using enhanced chemiluminescence (Amersham ECL Prime WB detection kit, GE Healthcare).

Immunohistochemistry (IHC) of fat pads excised and fixed in 4% PFA was performed as previously described **(**Béréziat V et al, Am J Pathol 2011;179:2443-2453).

SUPPLEMENTARY DATA

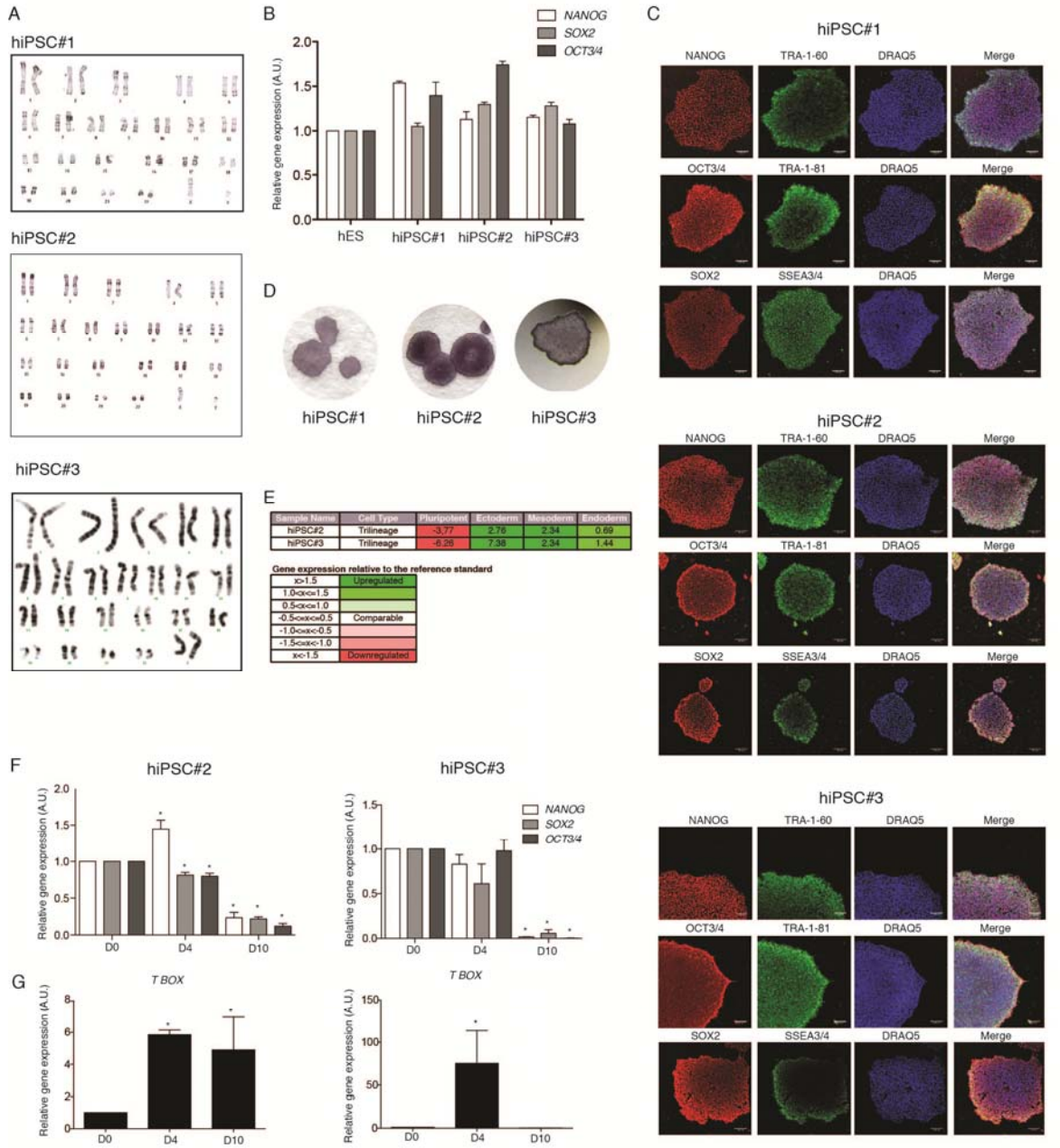
Supplementary Table 3. Primer sequences used for RT-quantitative PCR

CAR4	tgtccaaaataacgggcact	cagtcctcctccagaaatgc
C/EBPα	gacatcagcgcctacatcg	ggctgtgctggaacaggt
C/EBPβ	ccagccccctcactaatagc	ccctgctctgagctgtcg
C/EBPδ	ggacataggagcgcaaagaa	ggacataggagcgcaaagaa
CD137	agctgttacaacatagtagccac	tcctgcaatgatcttgtcctct
CD24	tgaagaacatgtgagaggtttgac	gaaaactgaatctccattccacaa
CD29	cgatgccatcatgcaagt	acaccagcagccgtgtaac
CD44	tgccgctttgcaggtgtat	ggcctccgtccgagaga
CITED1	accggacttggagtcagaga	cagtttcgccacctgaaaac
GAPDH	agccacatcgctcagacac	gcccaatacgaccaaatcc
DIO2	cctcctcgatgcctacaaac	gctggcaaagtcaagaaggt
EPST1	aggcaaaagtcaaccaggtg	tgaaggccagataggagtcaa
HOXC9	gcagcaagcacaaagagga	cgtctggtacttggtgtaggg
KCNK3	ccttctacttcgccatcacc	gaacatgcagaacaccttgc
MYF5	ctatagcctgccgggaca	tggaccagacaggactgttacat
MTUS1	atctcaaggcagctttccacg	tcgcttgttgactttcgactc
NANOG	atgcctcacacggagactgt	cagggctgtcctgaataagc
OCT3/4	gcttcaagaacatgtgtaagctg	agggtttccgctttgcat
PAX7	gaaaacccaggcatgttcag	gcggctaatcgaactcactaa
PDGFRα	ccacctgagtgagattgtgg	tcttcaggaagtccaggtgaa
PGC1α	tgagagggccaagcaaag	ataaatcacacggcgctctt
PPARα	gcactggaactggatgacag	tttagaaggccaggacgatct
PPARγ	cagtggggatgtctcataa	cttttggcatactctgtgat
PRDM16	tggctgcttctggactca	atattatttacaacgtcaccgtcact
Sca-1/LY6E	gccatcctctccagaatgaa	gcaggagaagcacatcagc
SOX2	gggggaatggaccttgtatag	gcaaagctcctaccgtacca
T BOX	gctgtgacaggtacccaacc	catgcaggtgagttgtcagaa
TMEM26	ttgcaccatgagacccagt	tgctggtattctgtgatgttcc
UCP1	ctcaccgcagggaaagaa	ggttgcccaatgaatactgc

Total RNAs were extracted with NucleoSpin RNA (Macherey-Nagel) according to the manufacturer instructions. cDNA was synthetized from 1 µg RNA (High capacity cDNA reverse transcription kit, Life Technologies). Quantitative PCR was performed with LightCycler 480 using LightCycler 480 SYBR Green I Master mix (Roche Diagnostics). GAPDH mRNA was used for normalization.

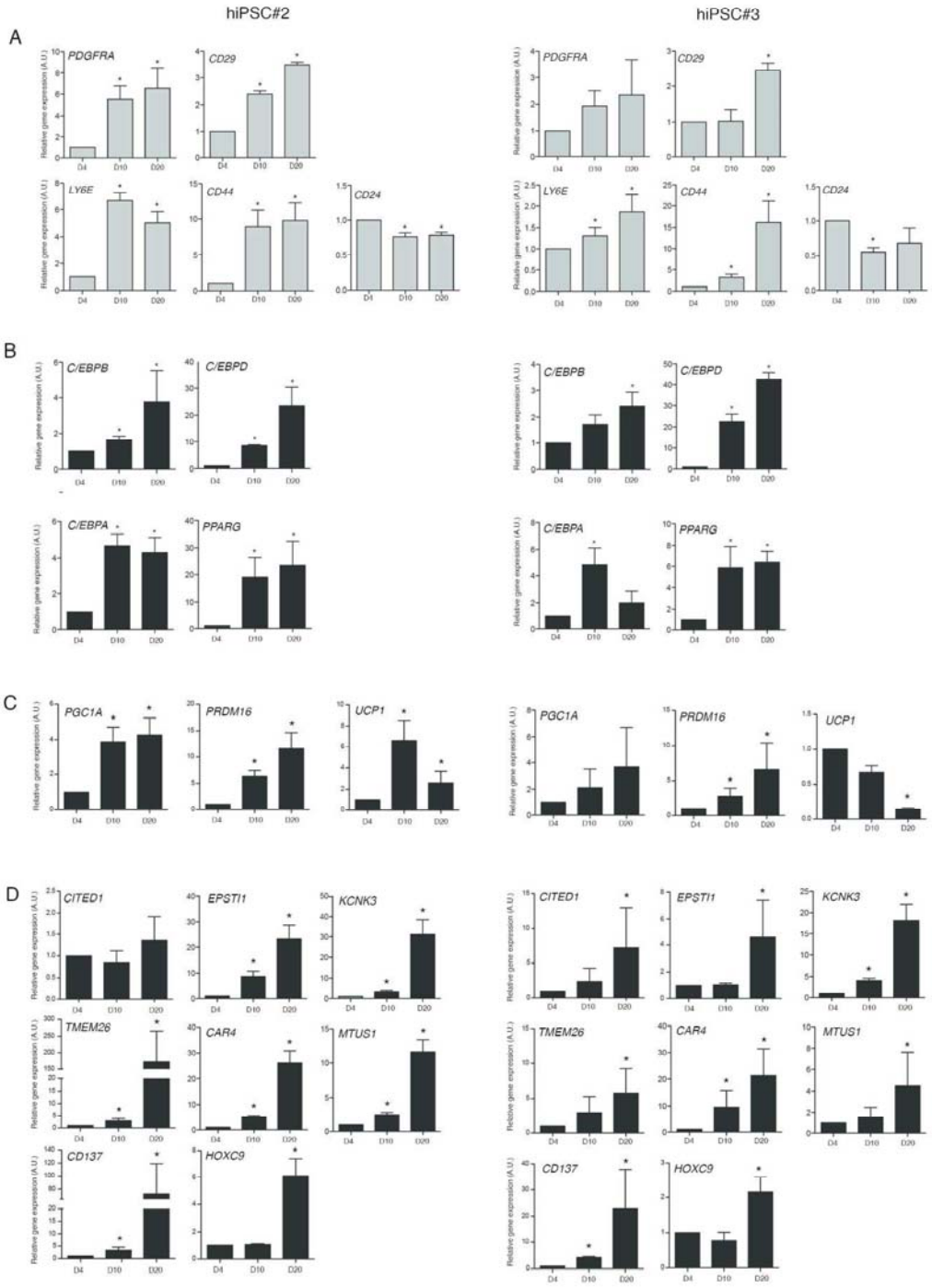
SUPPLEMENTARY DATA

Supplementary Figure 1. Characterization of pluripotency and mesodermal differentiation of hiPSC
Characterization of hiPSC at D0 for (**A**) normal karyotype, (**B**) *NANOG SOX2* and *OCT3/4,* mRNA gene expression compared to that of human embryonic stem cells (ESC) (mean ± SEM arbitrary units (A.U.) relative to D0; n ≥ 3 independent experiments; *p<0.05 relative to D0, Mann-Whitney U-test). (**C**) Immunostaining of NANOG, OCT4, SOX2 (red), TRA-1-60, TRA-1-81 and SSEA3/4 (green). Nuclei were stained with DRAQ5 (blue). Bars: 100 µm. (n≥3). (**D**) Positive alkaline phosphatase staining (using SIGMAFAST BCPI/NBT (Sigma-Aldrich) after fixation in 95% ethanol), and (**E**) Score Cards analysis (TaqMan® hPSC Scorecard™ Panel, Life Technologies) assessing pluripotency and trilineage differentiation potential of hiPSCs. Time-course mRNA expression analysis of the pluripotency markers *NANOG*, *SOX2* and *OCT3/4* (**F**) and the mesodermal transcription factor *T-brachyury* (*T BOX*) (**G**) (mean ± SEM A.U. relative to D0; n ≥ 3 independent experiments; *p<0.05 relative to D0, Mann-Whitney U-test).



SUPPLEMENTARY DATA

Supplementary Figure 2. Time course mRNA expression of hiPSC#2 and #3
(**A**) hiPSC#2 and hiPSC#3-derived adipocytes were characterized at D4 and after adipogenic induction (D10, D20). Time-course mRNA expression analysis of (**A**) *PDGFRA, LY6E*, *CD24, CD44, CD29* and (**B**) *C/EBPB*, *C/EBPD*, *C/EBPA* and *PPARG*. (**C**) brown/beige adipocyte markers *UCP1*, *PGC1A* and, *PRDM16,* and (**D**) beige adipocyte specific genes *CITED1, TMEM26, CD137, HOXC9*, *EPSTI1*, *CAR4*, *KCNK3* and *MTUS1* (mean ± SEM A.U. relative to D4; n ≥ 3 independent experiments; *p<0.05 relative to D4, Mann-Whitney U-test).



SUPPLEMENTARY DATA

Supplementary Figure 3. Global transcription analysis of the hiPSC-derived population during differentiation

(**A**) Unsupervised data analysis by principal component analysis (PCA) showing different patterns at each differentiation step. RNA concentration and integrity were evaluated with the Agilent Bioanalyzer 2100, and data were RMA (Robust Multi-array Average) normalized with Bioconductor. We used one-way ANOVA for time factor to extract DEGs with PartekGS©. N=3 independent experiments. (**B**) Heatmap and hierarchical clustering of the whole gene set at five successive stages of hiPSC-derived time course differentiation ($p<0.01$ over time). (**C, D, E**) Detailed heatmaps showing transcriptomic signatures of published datasets used for Gene Set Enrichment Analysis in Fig. 1. Gene Set Enrichment Analysis (www.broadinstitute.org/GSEA) used parameters of 1,000 gene set permutation, gene set size between 20 and 500 and weighted set. An enrichment map was generated using enriched gene set with $p<0.001$, FDR<1 and NES>5.