Supplementary Information

Loss of the transcription factor MAFB limits β-cell derivation from human PSCs

Russell et al.







Supplementary Figure 1. MAFB is expressed in hESC derived β-cells.

(A) Representative IF images from 4 independent experiments of INS-GFP cells at the β -cell stage depicting C-PEP, NKX6.1, MAFB and DAPI. Scale bars, 50 μ m.

(B) Representative IF images from 3 independent experiments from the β -cell stage of differentiation depicting C-PEP and MAFB expression in MAFB +/+, +/- and -/- cells. DAPI indicates nuclear staining. Scale bars, 50 μ m.



Supplementary Figure 2. Loss of MAFB inhibits β-cell derivation.

(A) Representative FC plots depicting the percentages of SOX17+ FOXA2+ at the DE stage for individual clones.

(B) Representative FC plots depicting the percentages of PDX1+ NKX6.1+ at the PP stage for individual clones.

(C) Representative FC plots depicting the percentages of GFP+ cells at the β -cell stage for individual clones.

(D) Representative FC plots depicting the percentages of C-PEP+ NKX6.1+ cells at the β -cell stage for individual clones.

(E) Quantification of GFP+ cells for individual clones the β -cell stage.

(F) Representative histograms and (G) Mean fluorescence intensity (MFI) of the GFP positive population in MAFB +/+, +/- and -/- cells. P values by one-way ANOVA followed by Dunnett's multiple comparisons test were ***P <0.0004 ****P < 0.0001. N = 6 independent experiments.

(H) Stimulation index of MAFB +/+ cells at 5 weeks post-transplantation. N = 3 independent mice.

(I) Total C-PEP content from individual clones at the β -like cell stage. N = 6 independent experiments.

P values by one-way ANOVA followed by Dunnett's multiple comparisons test were *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001. Data are presented as individual biological replicates and represent the mean \pm SD.



Supplementary Figure 3. MAFB is important for β -cell derivation.

(A) Representative images from 6 independent experiments at the DE stage of differentiation depicting SOX17 and FOXA2 staining. Scale bars, 50 μ m.

(B) Representative images from 6 independent experiments at the PP stage of differentiation depicting PDX1 and NKX6.1 staining. Scale bars, 50 µm.

(C) Representative images from 6 independent experiments at the β -like cell stage of differentiation depicting C-PEP co-staining with PDX1 and NKX6.1. Scale bars, 50 μ m.



Supplementary Figure 4. MAFB is required to generate functional β-cells *in vivo*.

Representative IF images from 6 independent animals (3 MAFB+/+ and 3 MAFB-/-) for C-PEP co-staining with PDX1 and NKX6.1 of grafts removed from kidney capsules 8 weeks post-transplantation. The graft is delineated and marked from the kidney using dashed lines. Scale bars, 100 μ m.



Supplementary Figure 5. scRNA sequencing reveals MAFB-/- generate Pancreatic Progentior cells in equivalent manner to MAFB+/+ cells.

(A) UMAP plot of MAFB +/+ and -/- cells at the PP stage of differentiation, color-coded by cell populations.

(B) UMAP projections of the integrated analysis of MAFB +/+ and -/- cells at the PP stage, colorcoded by genotype (left) and normalized PDX1 and NKX6.1 expression (middle, right).

(C) Scatter plot showing the average gene expression (log scale) for MAFB +/+ and -/- cells at the PP cell stage. No genes are significantly differentially expressed (log fold change >0.5, adjusted p value < 0.1) between MAFB +/+ and -/- cells. P value calculated with MAST test.

(D) The relative mRNA expression patterns in MAFB +/+ and -/- cells of designated genes for pan-pancreatic (*PDX1, PTF1A, SOX9* and *HNF6*) or pro-endocrine (*NGN3, NKX6.1, NKX2.2* and *NEUROD1*) at the PP stage as measured by quantitative PCR analysis. Each data point represents an independent biological sample.

(E) The mRNA expression patterns of designated genes for individual clones for pancreatic (*PDX1, PTF1A, SOX9* and *HNF6*) or pro-endocrine genes (*NGN3, NKX6.1, NKX2.2* and *NEUROD1*) at the PP stage as measured by quantitative PCR analysis. Each data point represents an independent biological sample.

P values by unpaired two-tailed t-test were *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001. Data are presented as individual biological replicates and represent the mean \pm SD.



Supplementary Figure 6. scRNA sequencing reveals MAFB regulates endocrine cell lineage commitment.

(A) Violin plot of CHGA gene expression (normalized) in the merged MAFB +/+ and -/- cells from **Figure 4A**, color-coded by cell populations.

(B) UMAP plot of MAFB +/+ and -/- cells at the β -like cell stage of differentiation color-coded by cell identity.

(C,D) UMAP visualization of the log-transformed, normalized expression of selected genes at t he β -like cell stage of differentiation in (C) MAFB+/+ and (D) MAFB-/- cells.



Supplementary Figure 7. MAFB regulates endocrine hormone producing-cell lineage commitment.

(A) Violin plot showing the expression of the top 5 genes and that are differentially expressed (Up and down regulated; fold change > 0.5, adjusted p value < 0.1) between MAFB +/+ and -/- cells in the β -like cell stage as well as the control endocrine genes *CHGA* and *GHRL*.

(B) The mRNA expression patterns of designated genes for individual clones for pro-endocrine (*NGN3*, *NKX6.1*, *NKX2.2* and *NEUROD1*) stages and islet hormones (*INS*, *GCG*, *SST*, *PPY* and *GHRL*) at the β -like cell stage as measured by quantitative PCR analysis. Each data point represents an independent biological sample.

(C) The mRNA expression patterns of genes implicated in endocrine cell fate (*PAX4*, *PAX6*, *HHEX*, *ARX*, *CHGA* and *MAFA*) as well as the β -cell de-differentiation marker *ALDH1A3* at the the β -like cell stage as measured by quantitative PCR analysis. Each data point represents an independent biological sample.

P values by unpaired two-tailed t-test were *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001. Data are presented as individual biological replicates and represent the mean \pm SD.

Top 5 downregulated genes

Top 5 upregulated genes



Supplementary Figure 8. MAFB occupies α - and β -cell specific genes.

ChIP-seq binding profiles for MAFB at the indicated *gene loci* in Human Islet Pancreas ^{1,2} and EndoC-BH2 cells. Tracks are set to the same scale for HIP and EndoC-BH2 cells per gene and the lengths of genes and direction of transcription are indicated by blue arrows. The top 5 up- and down-regulated genes identified in our MAFB +/+ and -/- β -cell differentiations in **Figure 4B** are outlined.







Supplementary Figure 9. MAFB regulates differentiation of islet-hormone producing cell types.

(A) Representative FC plots depicting the percentages of C-PEP+ CHGA+ cells for individual clones at the β -like cell stage.

(B) Representative FC plots depicting the percentages of CHGA+ GCG+ cells for individual clones at the β -like cell stage.

(C) Representative FC plots depicting the percentages of C-PEP+ GCG+ cells for individual clones at the β -like cell stage.

(D) Representative FC plots depicting the percentages of C-PEP+ SST+ cells for individual clones at the β -like cell stage.

(E) Representative FC plots depicting the percentages of KI67+ cells at the PP and β -cell stage and respective quantification (n=3).

(F) Representative IF images from 3 independent experiments of MAFB +/+ and -/- cells at the PP and β -cell stage depicting NGN3, KI-67 and DAPI. Scale bars, 50 μ m.

(G) Representative IF images from 6 independent animals (3 MAFB+/+ and 3 MAFB-/-) for SST costaining with GCG (upper panel) and PPY (lower panel) of grafts removed from kidney capsules 8 weeks post-transplantation of MAFB +/+ and -/- cells. The graft is delineated and marked from the kidney using dashed lines where indicated. Scale bars, 50 μ m.

Α



В



MAFB +/+ MAFB -/GC

С

Supplementary Figure 10. MAFB directs Pancreatic Endocrine cell lineage specification.

(A) Representative IF images from 3 independent experiments the β -cell stage of differentiation depicting GCG, SST, NKX6.1 and DAPI. Scale bars, 50 μ m.

(B) Representative IF images from 3 independent experiments the β -like cell stage of differentiation depicting SST and HHEX and DAPI. Scale bars, 50 μ m.

(C) Representative IF images from 3 independent experiments the β -like cell stage of differentiation depicting PPY and GCG and DAPI. Scale bars, 50 μ m.



Supplementary Figure 11. Rescue of MAFB in MAFB-/- cells.

(A) Schematic outlining gene rescue and temporal control of *MAFB* expression in *MAFB*-/-hESCs.

(B) Representative FC plots depicting the percentages of C-PEP+ NKX6.1+ cells at the β -cell stage.

(C) Representative FC plots depicting the percentages of C-PEP+ SST+ cells at the β -cell stage.

(D) Representative FC plots depicting the percentages of PDX1+ NKX6.1+ cells at the β -cell stage.

(E) Quantification of data from B,C,D (n = 3).

(F) Representative histograms and (G) Mean fluorescence intensity (MFI) of the GFP positive population in -DOX and +DOX treated cells (n = 3).

P values by paired two-tailed t-test were *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001. Data are presented as individual biological replicates and represent the mean \pm SD.



Ε

Supplementary Figure 12. MAFB is critical to β -cell identity.

(A - E) Representative IF images from 3 independent experiments at the DE, PP and β -like cell stages of differentiation for the respective markers as indicated. Scale bars, 50 μ m.

shRNA Control

Α



DAPI

mCherry

MAFB

В





Merge

Merge





Supplementary Figure 13. MAFB is important for β-cell identity in EndoC-βH2 cells.

(A) The mRNA expression patterns of indicated genes for pancreatic and islet cell subtypes in EndoC- β H2 cells with shRNA control or MAFB knockdown as measured by quantitative PCR analysis (n=3).

(B) Representative IF images of EndoC- β H2 cells with shRNA control or MAFB depicting MAFB, mCherry and DAPI one week post lentiviral transduction. Scale bars, 50 μ m.

(C) Representative IF images of EndoC-βH2 cells with shRNA control or MAFB depicting SST, INS, mCherry/GFP and DAPI one week post lentiviral transduction. Scale bars, 50 μm.

P values by paired two-tailed t-test were *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001. Data are presented as individual biological replicates and represent the mean \pm SD.







Supplementary Figure 14. Characterization of human α -cell differentiation from INS-GFP hESCs.

(A) Representative FC plots depicting the percentages of GCG+ C-PEP+ cells, GCG+ NKX2.2+ and ARX+ cell at the indicated stages of α -cell differentiation in INS-GFP cells.

(B) Quantification of FC data from A (n=3).

(C) Representative IF images from 3 independent experiments from differentiating α -cells depicting GCG, INS and ARX (top panel) and SST, NKX6.1 and PDX1 (lower panel) at D26. Scale bars, 50 μ m.

(D) The mRNA expression patterns of islet hormones throughout α -cell differentiation at the indicated timepoints as measured by quantitative PCR analysis. Top panel – parental INS-GFP cell line. Lower panel – MAFB +/+ and -/- differentiations. (n=3).

P values by paired two-tailed t-test were *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001. Data are presented as individual biological replicates and represent the mean \pm SD.







Supplementary Figure 15. Loss of MAFB limits α -cell differentiation.

(A,B) Representative IF images from 3 independent experiments at the α -cell stage depicting GCG, INS and ARX and PDX1, SST and NKX6.1 in d26 α -cells from MAFB +/+ and -/- differentiations. Scale bars, 50 μ m.

(C) Quantification of GCG secretion in response to low and high glucose from MAFB +/+ and -/- cells at d26-34 *in vitro*. 3 independent experiments are shown.

В



Uncropped immunoblots from Figure 1



D MAFB 37 kDa - Vinculin 100 kDa -

Uncropped immunoblots from Figure 4

Uncropped immunoblots from Figure 5



Gating Strategy for Flow Cytometry Analysis

- (A-D) Uncropped western blots.
- (E) Flow Cytometry gating strategy.

Supplementary References:

- 1 Pasquali, L. *et al.* Pancreatic islet enhancer clusters enriched in type 2 diabetes riskassociated variants. *Nat Genet* **46**, 136-143, doi:10.1038/ng.2870 (2014).
- 2 Mularoni, L., Ramos-Rodriguez, M. & Pasquali, L. The Pancreatic Islet Regulome Browser. *Front Genet* **8**, 13, doi:10.3389/fgene.2017.00013 (2017).

Day	Media compo	nents			
D0	DMEM/F-12	1xGlutamax	1xMEM-NEAA	1x 2-Mercaptoethanol	4% KSR
D1-5	RPMI	1xGlutamax			
D6-7	DMEM	1xGlutamax			
D8	DMEM	1xGlutamax			
D9-11	DMEM	1xGlutamax			
D12-20	DMEM	1xGlutamax			

Supplementary Table 1. hESC differentiation into β-like cells – Backbone Media Formulation

Day	Media	Supplement					
D0	Seed hESCs 5.5 million cells/ well in 6 well plates with D0 media						
	Day0	HERβ1	Activin A	FGF-2			
D1	Rinse cells with [)PBS (w/o C	a ²⁺ , Mg ²⁺) for	5 min and ac	dded Day 1 differentiation media		
	Day 1	FBS	Activin A	ITS	Wnt-3a		
	Day I	0.2%	100ng/ml	0.02X	50ng/ml		
D2	Day 2	FBS	Activin A	ITS			
02	Day 2	0.2%	100ng/ml	0.05X			
	Day 3	FBS	KGF	ITS	TGF-β IV		
80	Day 5	0.2%	25ng/ml	0.1X	2.5µM		
D4-5	Day 4-5	FBS	KGF	ITS			
810	Day 10	0.2%	25ng/ml	0.1X			
D6-7	Day 6-7	B27	TTNPB				
201	Dayor	1X	3nM				
D8	Dav 8	B27	TTNPB	EGF			
20	Day 0	1X	3nM	50ng/m			
D9-11	Day 9-11	B27	KGF	EGF			
50 11	Bayeri	1X	50ng/ml	50ng/m			
D12-20	Day 12-20	B27 1X Heparin 10 T3 136ng/n Vitamin C 5	N-acetly I ug/ml Zine nL LDN 500µM	₋-cysteine 1m c sulfate 10µl N 500nM	hM NEAA 1X M Alk5i II 10uM XXi 2μM		

Supplementary Table 2. hESC differentiation into β-like cells – Media components

Supplementary Table 3. CRISPR gRNA target sequences for targeting MAFB.

Gene + guide no	gRNA Target sequence	РАМ
MAFB gRNA_1	GGTGTGTCTTCTGTTCGGTC	GGG
MAFB gRNA_2	TCTTCACGTCGAACTTGCGC	AGG
MAFB gRNA_3	ACACGGAGTGCTGAGCGGTG	TGG

Supplementary Table 4. PCR and sequencing primers used for genotyping and sequencing

Primer	Sequence (5'to 3')			
MAFB Seq Forward	GTGGAGAGGCAAGCGGAG			
MAFB Seq Reverse	GGGTTCATCTGCTGGTAGT			

Supplementary Table 5. Clonal Cell line sequence information.

Clone Name INS-GFP cells	Allele 1	Allele 2	Mutation	MAFB
E9	TACACGGAGTGCTGAGCGGTGTGG	TACACGGAGTGCTGAGCGGTGTGG	WT / WT	+/+
C8	TACACGGAGTGCTGAGCGGTGTGG	TACACGGAGTGCTGAGC TACACGGAGTGTGGAGCTACACGGAGCTACACGGA -GTGTGG	WT / 35bp insertion, 1bp deletion	+/-
D7	TACACGGAGTGCTGAGCGGTGTGG	TACACGGAGTGCTGAG	WT / 11bp deletion	+/-
E8	TACACGGAGTGCTGAGCGGTGTGG	TACACGGAGTGCTGAGCGG GTGTGG	WT / 1bp insertion	+/-
C9	TACACGGAGTGCTGAG	TACACGGAGTGCTGAGCGG GTGTGG	11 bp deletion / 1bp insertion	-/-
C10	TACACGGAGTGCTGAG	TACACGGAGTG TGTGG	10 bp deletion / 10 bp deletion	-/-
D9	TACACGGAGTGCTGAGCGG GTGTGG	TACACGGAGTGCTGAGCGG GTGTGG	1 bp insertion / 1 bp insertion	-/-

iPSCs	Mutation	MAFB
WT	WT / WT	+/+
Het	WT / 1bp insertion	+/-
KO	-83bp / -83bp	-/-

Supplementary Table 6. Differentially Expressed genes from MAFB +/+ and -/- cells at the beta-like stage (P_adj<0.1, FC>0.5)

Upregulated	Gene	avg_logFC	p_val_adj
1	GAST	2.316356715	5.47E-303
2	SST	2.041943535	3.41e-312
3	PPY	1.413802582	2.66E-86
4	PYY	0.855968146	5.21E-40
5	ISG15	0.708019373	2.08E-106
6	LY6E	0.70691153	1.69E-110
7	CGA	0.694610481	5.11E-26
8	TPPP3	0.687042188	2.92E-55
9	RGS4	0.677778669	6.87E-62
10	HSPA1B	0.669118669	6.82E-128
11	KCTD12	0.627579284	4.84E-73
12	FXYD2	0.600230106	2.50E-15
13	APOC1	0.561225169	1.98E-50
14	CTSB	0.554216445	4.72E-66
15	HSPA1A	0.549208538	2.61E-62
16	TIMP3	0.53469464	5.92E-48
Downregulated	Gene	avg_logFC	p_val_adj
1	GCG	-2.014125141	2.97E-196
2	INS	-1.934440177	0
3	CRYBA2	-1.931697312	7.71E-270
4	TTR	-1.227343372	4.19E-141
5	ACVR1C	-1.202830614	8.46E-202
6	SLC30A8	-0.964682775	3.13E-147
7	PPP1R1A	-0.829768652	1.25E-177
8	MT1G	-0.789324756	5.68E-20
9	PCP4	-0.767236561	4.91E-23
10	STMN2	-0.766230297	6.22E-121
11	NPTX2	-0.688057809	6.09E-95
12	COL5A2	-0.680313646	5.13E-49
13	MT2A	-0.655040748	2.85E-09
14	HMGB3	-0.641933516	2.24E-137
15	EPHX1	-0.638270828	1.44E-161
16	HADH	-0.638030748	8.31E-132
17	MT1X	-0.601419028	3.06E-25
18	ERO1LB	-0.596307901	7.24E-46
19	NEUROD1	-0.574711197	3.39E-93
20	CRISPLD1	-0.546023471	1.81E-74
21	NKX6-1	-0.54402969	8.58E-86
22	GAL	-0.537813148	2.19E-28
23	AIF1	-0.536504473	1.62E-127
24	SLC7A8	-0.536149322	1.43E-122
25	SNORA76	-0.509134644	8.98E-136
26	RP11-788H18.1	-0.504352542	5.51E-105

Supplementary Table 7. Differentially Expressed genes from MAFB +/+ and -/- cells in INS NKX6.1 high (Beta-like) cells at D20 (P_adj<0.1, FC>0.5)

	Gene	avg_logFC	p_val_adj
	SST	1.7366719	1.96E-60
	GAST TDO2	1.66897755	3.46E-35
	GIP	1.13050186	0.00014082
	DLK1	1.11721996	3.94E-13
	CALB2	1.04430784	3.19E-19 2.42E-23
	DDC	1.01089582	1.35E-25
	KCTD12	0.99970662	4.50E-23
	RGS4 WIS	0.9782056	1.94E-13 6 22E-30
	APOB	0.94060072	2.25E-10
	PYY	0.90482411	5.19E-08
	RGS2 HSPA1R	0.87481822	1.48E-18 2.87E-22
	IGFBP3	0.84857646	9.44E-15
	ISG15	0.82724423	5.18E-17
	FEV GUCY2C	0.81770723	3.27E-09 4.64E-14
	RAMP1	0.80390259	2.45E-13
	C15orf48	0.79627586	2.56E-30
	HSPA1A CXCL12	0.79213823	6.01E-11 4.10E-16
	PAM	0.76879532	3.18E-19
	SEZ6L	0.75968371	4.28E-27
	FXYD2 CHGA	0.75562301	0.00166/28 1.63E-25
	ASCL1	0.69631919	0.00012541
	MAFB	0.68021658	6.96E-14
	RGS9 GCH1	0.68020767	2.00E-22 2.87E-21
	RP11-279F6.1	0.65388567	6.65E-09
	WFDC2	0.65133335	2.86E-16
	HSPB1 IFI6	0.64429653	2.8/E-12 7.07E-25
	CLDN3	0.63748219	8.09E-21
	AC009014.3	0.61817642	1.89E-16
	C12orf75	0.61341069	8.35E-14 2.97E-16
	PTPRN	0.59283695	4.94E-23
	LINC00261	0.58999555	1.71E-09
	ETV1 CVBA	0.58263018	3.27E-13 1.21E-17
	FAM46B	0.57774928	1.81E-14
	LY6H	0.57595111	5.92E-10
	HLA-C	0.5571406	1.29E-17
	MT-ND4L	0.55588667	1.66E-14
	SPINK1	0.54124436	2.16E-07
	MDK	0.54081909	1.21E-06 1.66E-21
	RAB3B	0.53256072	1.68E-11
	APOE	0.53055919	3.72E-12
	NAV2	0.52619448	1.44E-14
	31.11/	11 2 19314112	
	TMSB4X	0.51930402	4.90E-05
	TMSB4X DSP	0.51930402 0.51453668 0.50794817	4.90E-05 2.14E-10
	TMSB4X DSP LCOR	0.51930402 0.51453668 0.50794817 0.50065824	1.50E-05 4.90E-05 2.14E-10 1.24E-19
	TMSB4X DSP LCOR	0.51930402 0.51453668 0.50794817 0.50065824	1.50E-05 4.90E-05 2.14E-10 1.24E-19
Downregulated	TMSB4X DSP LCOR	0.51950402 0.51453668 0.50794817 0.50065824	1.30E-05 4.90E-05 2.14E-10 1.24E-19
Downregulated	TMSB4X DSP LCOR TTR CRYBA2	-2.1840245 -2.0521569	2.48E-52 4.90E-05 2.14E-10 1.24E-19
Downregulated	TMSB4X DSP LCOR TTR CRYBA2 SLC30A8	-2.1840245 -1.7606669	1.50E-03 4.90E-05 2.14E-10 1.24E-19 2.48E-52 4.99E-67 1.60E-42
Downregulated	TTR DSP LCOR TTR CRYBA2 SLC30A8 MT1G NFFM	0.51453662 0.51453668 0.50794817 0.50065824 -2.1840245 -2.0521569 -1.7606669 -1.4277739 -1.313693	4.90E-05 4.90E-05 2.14E-10 1.24E-19 2.48E-52 4.99E-67 1.60E-42 0.0097721
Downregulated	TMSB4X DSP LCOR TTR CRYBA2 SLC30A8 MT1G NEFM GCG	0.51453668 0.50794817 0.50065824 -2.1840245 -2.0521569 -1.7606669 -1.4277739 -1.3136923 -1.0470691	1.50E-05 4.90E-05 2.14E-10 1.24E-19 2.48E-52 4.99E-67 1.60E-42 0.0097721 1.40E-11 4.83E-36
Downregulated	TTR TMS84X DSP LCOR TTR CRYBA2 SLC30A8 MT1G NEFM GCG MT1X	0.51453668 0.50794817 0.50065824 -2.1840245 -2.0521569 -1.7606669 -1.4277739 -1.3136923 -1.0470691 -1.0106086	2.48E-52 4.90E-05 2.14E-10 1.24E-19 2.48E-52 4.99E-67 1.60E-42 0.0097721 1.40E-11 4.83E-36 0.03612605
Downregulated	TTR TMSB4X DSP LCOR TTR CRYBA2 SLC30A8 MT1G NEFM GCG GCG MT1X ACVR1C NPTY2	-2.1840245 -2.1840245 -2.0521569 -1.7606669 -1.4277739 -1.3136923 -1.010686 -1.0016424	2.48E-52 4.90E-05 2.14E-10 1.24E-19 2.48E-52 4.99E-67 1.60E-42 0.0097721 1.40E-11 4.83E-36 0.03612605 1.10E-46 1.55E-11
Downregulated	TTR TMSB4X DSP LCOR TTR CRVBA2 SLC30A8 MT1G NEFM GCG MT1X ACVR1C NPTX2 RT1X788H18.1	-2.1840245 -2.1840245 -2.0521569 -1.7606669 -1.4277739 -1.3136923 -1.0106086 -1.0016424 -0.9677836	2.48E-52 4.90E-05 2.14E-10 1.24E-19 2.48E-52 4.99E-67 1.60E-67 1.60E-67 1.60E-67 1.40E-11 4.83E-36 0.03612605 1.10E-46 1.55E-11 3.40E-22
Downregulated	TTR TMSB4X DSP LCOR TTR CRVBA2 SLC30A8 MT1G NEFM GCG MT1X ACVR1C NPTX2 RP11-788H18.1 HADH	0.51453668 0.50794817 0.50065824 -2.1840245 -2.0521569 -1.7606669 -1.4277739 -1.3136923 -1.0470691 -1.0106086 -1.0016424 -0.9677836 -0.9259451 -0.8920445	1.50E-05 4.90E-05 2.14E-10 1.24E-19 2.48E-52 4.99E-67 1.60E-42 0.0097721 1.40E-11 4.40E-11 4.40E-11 4.40E-11 1.00E-46 1.55E-11 3.40E-22 3.15E-22 3.15E-22
Downregulated	TTR TMSE4X DSP LCOR TTR CRYBA2 SLC30A8 MT1G NEFM GCG MT1X ACVR1C NPTX2 RP11-788H18.1 HADH RTN1 SMC2	0.51930402 0.5143568 0.50794817 0.50065824 -2.1840245 -2.0521569 -1.7606669 -1.4277739 -1.0470691 -1.0470691 -1.0470691 -0.09577836 -0.9259451 -0.0820445 -0.8826712 -0.8826712	1.502-05 4.902-05 2.14E-10 1.24E-19 2.48E-52 4.99E-67 1.60E-42 0.03612605 1.40E-11 4.83E-36 0.03612605 1.10E-46 0.03612605 1.10E-46 0.03612605 3.15E-22 6.72E-34 2.72E-16
Downregulated	TTR TMSB4X DSP LCOR TTR CRVBA2 SLC30A8 MT1G NEFM GCG GCG MT1X ACVR1C NPTX2 RP11-788H18.1 HADH RTN1 SMC2 ASPH	2.1840245 -2.1840245 -2.052156 -1.760669 -1.760669 -1.047061 -1.016086 -1.0016424 -0.957785 -0.8858712 -0.8858712 -0.8858712 -0.8858712	1.502-05 4.902-05 2.14E-10 1.24E-19 2.48E-52 4.99E-67 1.60E-42 0.0097721 4.405-11 4.4382-36 0.00912605 1.10E-46 1.55E-11 3.406-22 3.15E-22 6.72E-34 2.72E-16 9.22E-20
Downregulated	TTR TMSB4X DSP LCOR TTR CRYBA2 SLC30A8 MT1G NEFM GCG MT1X ACVR1C NPTX2 RP11-788H18.1 HADH RTN1 SMC2 ASPH EPHX1 CCGUZ	-2.1840245 -2.1840245 -2.0521569 -1.750665824 -2.0521569 -1.7506669 -1.4277739 -1.3136923 -1.0470691 -1.0106086 -0.9259451 -0.957785 -0.8855712 -0.8855474 -0.88554849714 -0.8531484 -0.8535148 -0.8535288	1.502-05 4.902-05 2.14E-10 1.24E-19 2.48E-52 4.99E-67 1.60E-42 0.0097721 1.40E-11 4.40E-11 4.40E-11 4.40E-11 3.40E-22 3.15E-22 6.72E-34 2.72E-16 9.22E-20 8.25E-28
Downregulated	3.G2 TMSB4X DSP LCOR TTR CRYBA2 SLC30A8 MT1G NEFM GCG MT1X ACVR1C NPTX2 RTN1-788H18.1 HADH RTN1 SMC2 ASPH EPHX1 PCDH7 EGFL7	0.51930402 0.51445366 0.50794817 0.50065824 -2.1840245 -2.0521569 -1.4277739 -1.0470691 -1.016424 -0.925945 -0.0925945 -0.0925945 -0.08286712 -0.8846714 -0.8846714 -0.8846714 -0.834631848 -0.83461754 -0.83461754 -0.8026577	1.502-03 4.902-05 2.14E-10 1.24E-19 1.24E-19 1.60E-42 0.0097721 1.40E-11 4.83E-36 0.03612605 1.10E-46 0.272E-16 0.272E-16 0.255E-11 1.20E-46 0.272E-16 0.255E-11 1.20E-46 0.272E-16 0.255E-16 0.25E-16 0.255E-
Downregulated	JLG2 4 TMSE44X DSP LCOR TTR CRYBA2 SLC30A8 MT1G SLC30A8 MT1G GCG MT1X ACVR1C NPTX2 RP11-788H18.1 HADH RTM1 SMC2 ASPH EPHX1 PCDH7 EGFL7 TLE4	-2.1840245 -2.1840245 -2.05065824 -2.05065824 -2.0521569 -1.4277739 -1.3136923 -1.047069 -1.016424 -0.9529451 -0.0829451 -0.0829451 -0.8384782 -0.8384784 -0.838488712 -0.8384784 -0.9384784454 -0.9384784454 -0.	1.502-05 4.902-05 2.14E-10 1.24E-19 2.48E-52 4.99E-62 1.60E-62 0.0097721 1.40E-11 4.83E-36 0.03612605 1.10E-64 1.55E-11 3.40E-22 3.15E-22 6.72E-34 2.72E-16 9.22E-20 8.25E-28 6.93E-17 1.78E-15 1.48E-14
Downregulated	TTR TMSB4X DSP LCOR TTR CRVBA2 SLC30A8 MT1G NEFM GCG MT1X ACVR1C NPTX2 RP11-788H18.1 HADH RTN1 SMC2 ASPH EPHX1 SMC2 ASPH EPHX1 EFL7 TLE4 HPCA	2.1840245 0.50794817 0.50065824 -2.1840245 -2.0521569 -1.7606669 -1.7606669 -1.0470679 -1.0470679 -1.0470679 -0.957785 -0.852044 -0.957785 -0.8531848 -0.758858 -0.	1.302-03 4.902-05 2.14E-10 1.24E-19 2.48E-52 4.995-67 1.60E-42 0.0097721 1.40D-11 4.83E-36 0.03612605 1.10E-64 0.03612605 1.10E-64 0.03612605 1.10E-64 0.03612605 1.10E-64 0.03E-17 0.22E-20 8.25E-28 6.93E-17 1.78E-15 1.48E-14 4.42E-28
Downregulated	TTR TMSB4X DSP LCOR TTR CRVBA2 SLC30A8 MT1G NEFM GCG MT1X ACVR1C NPTX2 RP11-788H18.1 HADH RTN1 SMC2 ASPH EPHX1 PCOH7 EGFL7 TLE4 HPCA AIF1 TUB82B	-2.1840245 -0.51445365 -0.50794817 -0.50065824 -2.0521569 -1.7606669 -1.060669 -1.0470671 -1.016086 -1.0016424 -0.9577845 -0.8858712 -0.7558815	2.48E-52 4.90E-05 2.14E-10 1.24E-19 2.48E-52 4.99E-67 1.60E-42 0.0097721 4.40E-11 4.438E-36 0.0097221 3.40E-21 3.40E-22 3.15E-22 3.15E-22 6.72E-34 2.72E-16 9.22E-20 8.25E-28 6.93E-17 1.78E-15 1.48E-14 4.32E-28
Downregulated	J.G2 TMSB4X TMSB4X DSP LCOR TTR CRVBA2 SLC30A8 MT1G NEFM GCG MT1X ACVR1C NPTX2 RTN1 SMC2 ASPH PT1-78BH18.1 HADH SMC2 ASPH PCH7 EGFL7 TLE4 HPCA AIF1 TUBB28 LBH	-2.1840245 0.51445366 0.50794817 0.50065824 -2.0521569 1.4277739 1.0470691 1.0106424 -0.925945 1.01016424 0.925945 1.01016424 0.925945 0.0849714 0.0858712 0.8849714 0.925945 0.0849714 0.925945 0.08489714 0.925945 0.08489714 0.925945 0.08489714 0.925945 0.08489714 0.925945 0.08489714 0.925945 0.08489714 0.925945 0.08489714 0.925945 0.08489714 0.925945 0.08489714 0.925945 0.08489714 0.925945 0.08489714 0.925945 0.09259450 0.09259450 0.09259450 0.0925945000000000000000000000000000000000	1.502-03 4.902-05 2.14E-10 1.24E-19 1.24E-19 1.60E-42 0.0097721 1.40E-11 4.83E-36 0.03612605 1.10E-46 0.03612605 1.10E-46 9.25E-18 4.83E-32 6.72E-34 7.72E-36 7.72E-3
Downregulated	JCG2 TMSE44X DSP LCOR TTR CRVBA2 SLC30A8 MTIG NEFM GCG MT1A ACVRIC NPTX2 PP11-788H18.1 HADH RTN1 SMC2 ASPH EPHX1 PCOH7 EGFL7 TLE4 HPCA AIF1 TUB828 LBH SLC25A5	-2.1840245 0.5145366 0.50794817 0.50065824 -2.0521569 -1.4277739 -1.3136923 -1.047069 -1.4277739 -1.3136923 -1.047069 -1.016424 -0.9259451 -0.016242 -0.8846712 -0.8846714 -0.88458712 -0.88458712 -0.88458712 -0.83458712 -0.83458712 -0.83458712 -0.83458712 -0.83458712 -0.83458712 -0.83458712 -0.83458712 -0.775681 -0.7755815 -0.7755815 -0.7755815 -0.7757581 -0.777761 -0.67717014 -0.67117014	1.302-03 4.902-05 2.14E-10 1.2
Downregulated	JCG2 TMSE44X DSP LCOR TTR CRYBA2 SLC30A8 MT1G NEFM GCG MT1X ACVR1C NPTX2 RP11-788H18.1 HADH RTM1 SMC2 ASPH EPHX1 PCDH7 EGFL7 TLE4 HPCA AJF1 TUBB2B LBH SLC2A5 SNORA76	-2.1340245 0.51445366 0.50794817 0.50065824 -2.0521569 -1.4277739 -1.3136923 -1.047069 -1.4277739 -1.3136923 -1.0106026 -1.0106424 -0.9677836 -0.925451 -0.0165424 -0.8384732 -0.83845712 -0.83845712 -0.83845712 -0.83845712 -0.83845712 -0.83845712 -0.83845712 -0.83845712 -0.83845712 -0.677836 -0.775614 -0.671104 -0.671104 -0.66743876	1.302-03 4.902-05 2.14E-10 1.24E-19 2.48E-52 4.99E-67 1.60E-42 0.0097721 1.40E-11 4.83E-36 0.03612605 0.03612605 0.03612605 1.10E-46 1.55E-11 3.40E-12 3.15E-22 6.72E-34 2.72E-16 9.22E-20 8.25E-28 4.48E-17 1.78E-15 1.48E-14 4.32E-28 1.30E-23 2.46E-17 1.68E-12 6.83E-20 1.85E-18 2.24EE-17 1.68EE-12 6.83E-20 1.85E-18 2.46E-17 1.68EE-12 6.83E-20 1.85E-18 2.46E-17 1.68EE-12 6.83E-20 1.85E-18 2.46E-17 1.68EE-12 6.83E-20 1.85E-18 2.46E-17 1.68EE-12 6.83E-20 1.85E-18 2.46E-17 1.68EE-12 6.83E-20 1.85E-18 2.46E-17 1.68EE-12 6.83E-20 1.85E-18 2.46E-17 1.68EE-12
Downregulated	TTR TMSE4X DSP LCOR TTR CRYBA2 SLC30A8 MT1G NEFM GCG GCG MT1X ACVR1C NPTX2 RP11-788H18.1 HADH RTN1 SMC2 ASPH EPHX1 EPHX1 EPHX1 EPHX1 EFL7 TLE4 HPCA AIF1 TUB82B LBH SLC25A5 HMGB3 SNORA76 STMNZ	0.51930402 0.5145366 0.50794817 0.50065824 -2.1840245 -2.0521569 -1.4277739 -1.3136923 -1.7606659 -1.4277739 -1.3136923 -1.047069 -1.016424 -0.9677836 -0.9259451 -0.016242 -0.8849714 -0.8859712 -0.8849714 -0.8853712 -0.8849714 -0.8853712 -0.8849714 -0.8853712 -0.8849714 -0.8853712 -0.8849714 -0.8853712 -0.7358968 -0.8853718 -0.7358968 -0.8161754 -0.7576144 -0.6771041 -0.6771041 -0.6712041 -0.6649367 -0.6643836	1.502-03 4.902-05 2.14E-10 1.24E-19 2.48E-52 4.99E-67 1.60E-42 0.0097721 1.40E-11 4.83E-36 1.10E-46 0.03612605 1.10E-46 9.03612605 1.10E-46 9.22E-20 8.25E-28 6.72E-34 2.72E-16 9.22E-20 8.25E-28 6.93E-17 1.78E-15 1.48E-14 4.32E-28 1.30E-23 2.46E-17 1.69E-12 6.83E-20 1.85E-18 2.98E-19 1.77E-21
Downregulated	TTR TMSE44X DSP LCOR TTR CRVBA2 SLC30A8 MT1G NEFM GCG MT1X ACVR1C NPTX2 RP11-788H18.1 HADH RTN1 SMC2 ASPH EFK1 PCDH7 EGFL7 TLE4 HPCA AIF1 VUB828 LBH SLC25A5 HMGB3 SNORA76 STMN2 ROB02 TIMESE71	2.1840245 0.51445365 0.50794817 0.50065824 2.05015824 1.7606669 1.7606669 1.4277739 1.3136923 1.0470691 1.0106086 1.0016424 0.967785 0.882047 0.882047 0.882047 0.883072 0.8836712 0.8836712 0.8836712 0.8836712 0.7756815 0.7755815 0.77558968 0.77558968 0.77558968 0.77558968 0.77558968 0.77558968 0.77558968 0.77558968 0.77558968 0.77558968 0.77558968 0.77558968 0.77558968 0.77558968 0.7552896 0.7	1.502-05 4.902-05 2.14E-10 1.24E-19 2.48E-52 4.995-67 1.60E-42 0.0097721 1.400E-11 4.83E-36 0.03612605 1.10E-46 0.03612605 1.10E-46 0.03612605 1.10E-46 9.22E-20 9.22E-20 9.22E-20 9.22E-20 8.25E-28 6.038:17 1.78E-15 1.48E-14 4.332E-28 1.305E-23 2.46E-17 1.685E-18 2.34E-19 1.55E-18 1.35E-12 1.48E-14 4.32E-28 1.305E-23 2.46E-17 1.685E-18 2.34E-19 1.55E-18 1.35E-18 2.34E-19 1.55E-18 1.35E-18
Downregulated	JUG2 TMSB4X DSP LCOR TTR CRVBA2 SLC30A8 MT1G NEFM GCG MT1X ACVR1C ACVR1C ACVR1C NPTX2 RTN1 SMC2 ASPH EPHX1 PCDH7 EGFL7 TLE4 HPCA AIF1 TUBB28 LBH SLC25A5 MMG83 SNORA76 STMN2 ROB02 TNFR5F21 HNRNPA1	-2.1840245 0.51445366 0.50794817 0.50065824 -2.0521569 -1.4277739 -1.3136923 -1.0470691 -1.016424 -0.925945 -0.0849714 -0.925945 -0.8849714 -0.925945 -0.8849714 -0.8849714 -0.88531848 -0.84849714 -0.83531848 -0.84849714 -0.7358156 -0.7358156 -0.7358156 -0.7358156 -0.7358156 -0.7358156 -0.7358156 -0.7358156 -0.7358156 -0.7358156 -0.7358156 -0.7358156 -0.7358156 -0.7358156 -0.7358156 -0.7358156 -0.7358156 -0.65493657 -0.65433057 -0.65433057 -0.65433057 -0.65433057	1.302-03 4.902-05 2.14E-10 1.24E-19 2.48E-52 4.99E-67 1.60E-42 0.0097721 1.40E-11 4.83E-36 0.03612605 1.10E-46 4.83E-36 0.03612605 1.10E-46 9.25E-28 4.83E-36 9.25E-28 4.93E-17 1.37E-12 1.37E-1
Downregulated	J.G.2 TMSE44X DSP LCOR TTR CRVBA2 SLC30A8 MT1G NEFM GCG MT1A ACVR1C NPTX2 RP11-788H18.1 HADH RTN1 SMC2 ASPH EPHX1 PCOH7 EGFL7 TLE4 HPCA JF1 SINORA76 STMM2 ROB02 TNFR\$52.1 HNRNPA11	0.51930402 0.5145366 0.50794817 0.50065824 -2.1840245 -2.0521569 -1.4277739 -1.3136923 -1.047069 -1.4277739 -1.016424 -0.9259451 -0.016242 -0.9259451 -0.016242 -0.9259451 -0.016242 -0.8846712 -0.8846714 -0.884674 -0.8362382 -0.8363124 -0.8363124 -0.8363124 -0.775681 -0.775681 -0.775681 -0.775581 -0.775581 -0.775581 -0.775581 -0.775581 -0.775581 -0.775581 -0.775581 -0.775681	1.302-03 4.902-05 2.14E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.40E-11 4.83E-36 0.03612605 1.10E-46 9.22E-20 8.25E-28 6.93E-17 1.78E-15 1.27E-16 9.22E-20 8.25E-28 6.93E-17 1.78E-15 1.48E-14 4.32E-28 1.30E-23 2.46E-17 1.66E-17 1.66E-17 1.66E-17 1.66E-17 1.66E-17 1.66E-17 1.66E-17 1.78E-15 1.66E-17 1.78E-15 1.78E-15 1.78E-15 1.78E-15 1.78E-15 1.78E-15 1.78E-15 1.78E-15 1.78E-15 1.78E-15 1.78E-15 1.78E-15 1.78E-15 1.78E-15 1.78E-15 1.78E-15 1.78E-15 1.78E-15 1.78E-15 1.77E-15 1.77E-15 1.77E-15 1.77E-21 5.77E-23 3.32E-17 2.04E-27 2
Downregulated	JLG2 TMSB4X DSP LCOR TTR CRYBA2 SLC30A8 MT1G NEFM GCG MT1A ACVR1C NPTX2 RP11-788H18.1 HADH RTM1 SMC2 ASPH EPHX1 PCDH7 EGFL7 TLE4 HPCA AIF1 TUB828 LBH SINORA76 STMR2 ROB02 TNFRSF21 HNRNPA1 ALDH1A1 FTL CH001	0.51930402 0.5145366 0.50794817 0.50065824 -2.1840245 -2.0521569 -1.4277739 -1.3136923 -1.047069 -1.4277739 -1.3136923 -1.010624 -0.9577836 -0.9577836 -0.9577836 -0.9577836 -0.9529451 -0.016424 -0.8384974 -0.8384974 -0.8384974 -0.8384974 -0.8384974 -0.8384974 -0.6381245 -0.6571404 -0.6541305 -0.65434054 -0.6544054 -0.654455 -0.654	1.302-03 4.902-05 2.14E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.60E-42 0.0097721 1.40E-11 4.83E-36 0.03612605 1.10E-46 1.55E-11 3.40E-22 6.72E-34 2.72E-16 9.22E-20 8.25E-28 6.93E-17 1.78E-15 1.32E-28 1.33E-22 6.83E-20 1.85E-18 2.24EE-17 1.68EE-12 6.83E-20 1.85E-18 2.98E-19 7.77E-21 5.72E-39 3.32E-17 2.04E-27 4.42E-09 5.93E-26 6.93E-17
Downregulated	JUG2 TTR TMSE44X DSP LCOR TTR CRYBA2 SUC30A8 MT1G NEFM GCG GCG MT1X ACVR1C NPTX2 RP11-788H18.1 HADH RTN1 SMC2 ASPH EPHX1 EFL7 TLE4 HPCA AIF1 TUB82B LBH SUC25A5 HMGB3 SNORA76 SSTMN2 ROB02 TNFRSF21 HNRNPA1 ALDH1A1 FTL CHODL NME1	0.51930402 0.5145366 0.50794817 0.50065824 -2.1840245 -2.0521569 -1.4277739 -1.3136923 -1.7606659 -1.4277739 -1.3136923 -1.047069 -1.0106124 -0.9677836 -0.9259451 -0.016242 -0.9826474 -0.8836712 -0.8836712 -0.8836714 -0.8836714 -0.8836714 -0.8836714 -0.7756815 -0.7358968 -0.876144 -0.671175 -0.6543035 -0.6543035 -0.6543035 -0.6543035 -0.6543035 -0.6543035 -0.6543035 -0.651525 -0.66315225 -0.66315225 -0.66315225 -0.66315225 -0.66315225 -0.66315225 -0.66315225 -0.66315225 -0.66315225 -0.663155 -0.663155 -0.655155 -0.65555 -0.655555 -0.6555555 -0.6555555 -0.65	1.302-03 4.902-05 2.14E-10 1.24E-19 2.48E-52 4.99E-67 1.60E-42 0.0097721 1.40E-14 4.83E-36 0.03612605 1.102-64 0.03612605 1.102-64 9.22E-07 8.25E-11 3.40E-22 6.72E-34 2.72E-16 9.22E-20 8.25E-28 6.93E-17 1.78E-15 1.48E-14 4.32E-28 1.30E-23 2.46E-17 1.68E-12 6.83E-20 1.85E-18 2.98E-19 7.77E-21 5.72E-39 3.32E-17 2.04E-2
Downregulated	JUG2 TTK TMSE44X DSP LCOR TTR CRVBA2 SLC30A8 MT1G NEFM GCG MT1X ACVR1C NPTX2 RTN1 SMC2 ACVR1C NPTX2 RTN1 SMC2 ASPH PCDH7 EGFL7 TLE4 HPCA AIF1 TUBB2B LBH SLC25A5 HMGB3 SNORA76 STMM2 RCB02 TNFR5F21 HNINPA1 ALDH1A1 FTL CHODL NMSE1 ANGPT2 ANGPT2	0.51343368 0.51445368 0.50794817 0.50065824 -2.1840245 -2.0521569 -1.4277739 -1.7606669 -1.4277739 -1.0470691 -1.016424 -0.925945 -0.016424 -0.925945 -0.016424 -0.925945 -0.016424 -0.8489714 -0.8489714 -0.8489714 -0.8489714 -0.8489714 -0.8489714 -0.8489714 -0.8489714 -0.8489714 -0.8489714 -0.756815 -0.7458495 -0.70121 -0.6797651 -0.66998967 -0.66440677 -0.66434054 -0.6131225 -0.631255 -0.631255 -0.55755 -0.631255 -0.55755 -0.631255 -0.55755 -0.631255 -0.55755 -0.631255 -0.55755 -0.631255 -0.55755 -0.631255 -0.55755 -0.631255 -0.55755 -0.55755 -0.55755 -0.55755 -0.55755 -0.55755 -0.55755 -0.557555 -0.557555 -0.5575555 -0.557555 -0.557555 -0.557555 -0.557555 -0.	1.302-03 4.902-05 2.14E-10 1.24E-19 1.24E-19 1.24E-19 1.60E-42 0.0097721 1.40E-11 4.83E-36 0.03612605 1.10E-46 9.22E-34 4.272E-16 9.22E-20 8.25E-28 4.272E-16 9.22E-20 8.25E-28 4.32E-2
Downregulated	JUG2 TTK TMSE44X DSP LCOR TTR CRVBA2 SLC30A8 MT1G NEFM GCG MT1X ACVR1C NPTX2 RF11-788H18.1 HADH RTN1 ACVR1C NPTX2 RF11-788H18.1 HADH RTN1 SMC2 ASPH EGFL7 TLE4 HPCA AIF1 TUB828 LBH SLC2SA5 HMGB3 STMN2 ROB02 TNFR5F21 HNRNPA1 ALCH1A1 FTL CHODL NME1 ANGPT2 PPP1R1A SURF4	0.15334402 0.1445366 0.50794817 0.50065824 -2.1840245 -2.0521569 -1.477739 -1.316923 -1.316923 -1.316923 -1.316923 -1.316923 -1.316923 -1.316925 -1.0016424 -0.9259451 -0.016244 -0.9259451 -0.016444 -0.9259451 -0.08849714 -0.08849714 -0.08849714 -0.08849714 -0.08849714 -0.08849714 -0.08849714 -0.08849714 -0.08849714 -0.08349745 -0.07576815 -0.7756815 -0.7756815 -0.7756815 -0.66494677 -0.65434054 -0.66494657 -0.66494356 -0.6649457 -0.6533555 -0.66303555 -0.66303577 -0.65322187 -0.5522187 -0	1.302-03 4.902-05 2.14E-10 1.24E-19 2.48E-52 4.99E-67 1.60E-42 0.0097721 1.40E-11 4.83E-36 0.03612605 1.102-46 4.83E-36 0.03612605 1.102-46 9.22E-20 8.25E-22 6.72E-34 2.72E-16 9.22E-20 8.35E-12 1.48E-14 4.32E-28 1.30E-23 2.46E-17 1.48E-14 4.32E-28 1.30E-23 2.46E-17 1.48E-14 4.32E-28 1.30E-23 2.46E-17 1.48E-14 4.32E-28 1.32E-21 2.48E-12 1.48E-14 1.32E-28 1.32E-21 2.48E-12 1.48E-14 1.32E-28 1.32E-21 2.48E-12 1.48E-14 1.32E-28 1.32E-21 2.48E-12 1.48E-14 1.32E-28 1.32E-27 1.48E-14 1.32E-28 1.32E-27 1.48E-14 1.48E-14 1.32E-28 1.32E-27 2.48E-17 1.48E-14 1.32E-28 1.32E-27 2.48E-17 1.48E-14 1.32E-28 1.32E-17 2.72E-19 3.32E-17 2.72E-13 2.72E-13 2.72E-13 2.72E-13 2.72E-13 2.72E-13 2.72E-13 2.72E-14 2.72E-16 1.55E-11 1.35E-11 1.55E-11 1.35E-1
Downregulated	JUG2 TTR TMSE44X DSP LCOR TTR CRVBA2 SLC30A8 MT1G NEFM GCG MT1X ACVR1C NPTX2 RP11-788H18.1 HADH RTN1 RTN1 SMC2 ASPH EPHX1 PCDH7 EGFL7 TUB42 SHC2 ASPH EPHX1 PCDH7 EGFL7 TUB4 HPCA AJF1 TUB828 LBH SLC25A5 STMN2 ROB02 TNFRSF21 HNRNPA1 ALDH1A1 FTL CHODL NME1 ANGPT2 PPP1R1A SURF4 SVIP	0.51930402 0.5145366 0.50794817 0.50065824 -2.1840245 -2.0521569 -1.4277739 -1.3136923 -1.047069 -1.4277739 -1.3136923 -1.016424 -0.957836 -0.8292445 -0.8292445 -0.82845712 -0.016424 -0.83845712 -0.775681 -0.775681 -0.775681 -0.775681 -0.775681 -0.775681 -0.775681 -0.775681 -0.775681 -0.775681 -0.775681 -0.6644367 -0.66443677 -0.654343054 -0.66315225 -0.6303177 -0.6392178 -0.5392178	1.302-03 4.902-05 2.14E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 2.25E-10 2.25E-10 2.25E-10 2.25E-28 6.93E-17 1.78E-15 1.32E-27 1.48E-14 4.32E-28 1.30E-23 2.46E-17 1.6683E-20 1.85E-18 2.98E-19 7.77E-21 5.72E-39 3.32E-17 2.04E-17 2.04E-17 2.04E-15 2.97E-21 2.03E-15 2.297E-21 2.03E-15 2.13E-22 2.97E-21 2.03E-15 3.13E-23 1.76E-17 3.82E-07
Downregulated	JUG2 TTR TMSE44X DSP LCOR TTR CRYBA2 SUC30A8 MT1G NEFM GCG MT1X ACVR1C NPTX2 RP11-788H18.1 HADH RTM1 SMC2 ASPH EPHX1 PCDH7 EGFL7 TUE4 HPCA AIF1 TUB82B LBH PCDH7 EGFL7 TUE4 HPCA AIF1 TUB82B LBH TUB82B SUC2AA5 STMN2 ROB02 STMN2 ROB02 STMR2 SURF7 SU	0.51930402 0.5145366 0.50794817 0.50065824 -2.1840245 -2.0521569 -1.4277739 -1.3136923 -1.4277739 -1.3136923 -1.047069 -1.0016424 -0.9677836 -0.957836 -0.957836 -0.959451 -0.016424 -0.8846714 -0.8846714 -0.8846714 -0.8363184 -0.8363184 -0.8363284 -0.8363284 -0.8363284 -0.775681 -0.775681 -0.775681 -0.775684 -0.675144 -0.675144 -0.675144 -0.675144 -0.6674365 -0.6434035 -0.6434035 -0.6434035 -0.6434035 -0.6434035 -0.6131225 -0.6039177 -0.5522187 -0.5745254 -0.57745254 -0.5777555 -0.57745254 -0.5774555 -0.577455 -0.577455 -0.577455 -0.577455 -0.577455 -0.5774555 -0.	1.302-03 4.902-05 2.14E-10 1.24E-19 1.24E-19 1.24E-19 1.24E-19 1.24E-19 1.24E-19 1.24E-19 1.24E-19 1.24E-19 1.24E-19 1.24E-19 1.24E-19 1.24E-19 1.24E-19 1.24E-19 1.24E-19 1.24E-19 1.24E-19 1.24E-19 2.25E-28 2.25E-28 2.25E-28 2.25E-28 2.25E-28 2.24EE-17 1.26E-12 2.35E-12 2.
Downregulated	JUG2 TTK TMSE44X DSP LCOR TTR CRVBA2 SLC30A8 MT1G NEFM GCG MT1X ACVR1C NPTX2 RTN1 SMC2 ASPH PT1-788H18.1 HADH SMC2 ASPH PT1-788H18.1 HADH SMC2 ASPH EFHX1 PCDH7 EGFL7 TLE4 HPCA AIF1 TUB82B LBH SLC25A5 HMG83 SNORA76 STMN2 ROB02 TNFR5F21 HMG83 SNORA76 STMN2 ROB02 TNFR5F21 HMS	0.15334402 0.1445366 0.50794817 0.50065824 -2.1840245 -2.0521569 -1.4277739 -1.0470651 -1.0106424 -0.925945 -1.0016424 -0.925945 -1.0016424 -0.925945 -0.925945 -0.925945 -0.8868712 -0.8868712 -0.8868712 -0.8868712 -0.8868712 -0.8868712 -0.8868712 -0.8868712 -0.8868712 -0.8868712 -0.8868712 -0.8868712 -0.8363184 -0.731876 -0.65672967 -0.6657294 -0.66592967 -0.6643055 -0.6303556 -0.6303556 -0.6303556 -0.5774554 -0.5743591 -0.5743551 -0.5743591 -0.54	1.302-03 4.902-05 2.14E-10 1.24E-19 1.24E-19 1.24E-19 1.60E-42 0.0097721 1.40E-11 4.83E-36 0.03612605 1.10E-46 9.22E-34 4.272E-16 9.22E-20 8.25E-28 6.93E-17 1.38E-15 1.48E-14 4.32E-28 6.93E-17 1.38E-12 1.48E-14 4.32E-28 6.93E-17 1.48E-14 4.32E-28 6.93E-17 7.77E-21 1.48E-14 4.32E-28 6.93E-17 7.77E-21 1.48E-14 4.32E-28 6.93E-17 7.77E-21 2.04E-27 2.97E-21 2.04E-27 2.97E-21 2.04E-27 2.97E-21 2.04E-27 2.97E-21 2.03E-15 3.13E-23 1.75E-17 3.32E-07 2.57E-21 2.38E-08 3.38E-08
Downregulated	JUG2 TTK TMSE44X DSP LCOR TTR CRVBA2 SLC30A8 MT1G NEFM GCG MT1X ACVR1C NPTX2 RFIN ACVR1C NPTX2 RTN1 SMC2 ASPH PCDH7 EGFL7 TLE4 HPCA AIF1 TUBB28 LBH SLC25A5 MMGB3 SNORA76 STMN2 ROB02 TNFR5F21 HMGB3 SNORA76 STMN2 ROB02 TNFR5F21 HNRNPA1 ALDH1A1 FTL CHODL NME1 ANGPT2 PPIXNA2 RAN PCSK2	0.51930402 0.5145366 0.50794817 0.50065824 2.0521569 1.4277739 1.0470691 1.010642 0.9259431 0.016642 0.925943 1.0106085 1.0106085 1.0106085 1.0106085 1.0106085 0.925943 0.08849712 0.08849714 0.08849714 0.08849714 0.08849714 0.08849714 0.08849714 0.08849714 0.08849714 0.08849714 0.0758415 0.08849714 0.0758415 0.0758415 0.0758455 0.067175 0.66440577 0.6643836 0.6107457 0.65434054 0.6593957 0.65431057 0.65921187 0.059	1.302-03 4.90E-05 2.14E-10 1.24E-19 1.24E-19 1.24E-19 1.60E-42 0.0097721 1.40E-11 4.83E-36 0.03612605 1.10E-46 9.25E-23 3.15E-22 3.25E-12 3.25E-23 3.32E-17
Downregulated	JUG2 TTR TMSE44X DSP LCOR TTR CRVBA2 SUC30A8 MT1G NEFM GCG MT1X ACVR1C NPTX2 RP11-788H18.1 HADH RTN1 ACVR1C NPTX2 RP11-788H18.1 HADH RTN1 SMC2 ASPH EPHX1 PCOH7 EGFL7 TUB42 HPCA AIF1 TUB828 LBH SUC2SA5 HMGB3 STMN2 ROB02 TNFR5F21 HNRNPA1 ALDH1A1 FTL CHODL NME1 ANGPT2 PPP1R1A SURF4 SURF5 SURF4 SURF5 SURF5 SURF5 SURF5 SURF5 SURF5 SURF5 SURF5 SU	0.51930402 0.5145366 0.50794817 0.50065824 2.0521569 1.4277739 1.3136923 1.047069 1.4277739 1.3136923 1.0106086 1.4277739 1.3136923 1.0106086 1.010642 0.9259451 0.08849714 0.08849714 0.08849714 0.08849714 0.08849714 0.08849714 0.08849714 0.08849714 0.08849714 0.08849714 0.08849714 0.08849714 0.08849714 0.08849714 0.08849714 0.08849714 0.08849714 0.0684805 0.0757851 0.0757851 0.0757494 0.6671377 0.66431057 0.6631272 0.6631272 0.6631272 0.6631272 0.6631272 0.5745545 0.6631272 0.5745545 0.053177 0.5745254 0.575524 0.5745254 0.575524 0.5745254 0.575524 0.575524 0.5745254 0.575524 0.5745254 0.575524 0.575524 0.5745254 0.575524 0.5745254 0.5745254 0.575524 0.5745254 0.5745254 0.5745254 0.5745254 0.5745254 0.5745254 0.5745254 0.5745254 0.5745254 0.5745254 0.5745254 0.5745254 0.5745254 0.5745254 0.57455	1.302-03 4.902-05 2.14E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.40E-11 4.83E-36 0.03612605 1.102-46 9.22E-20 8.25E-28 6.93E-17 1.78E-15 1.34DE-22 6.83E-20 8.25E-28 6.93E-17 1.78E-15 1.32E-28 6.93E-17 1.78E-15 1.32E-28 6.93E-17 1.78E-15 1.32E-28 6.93E-17 1.78E-15 1.32E-28 6.93E-17 1.78E-15 1.32E-17 2.04E-27 2.04E-27 2.04E-27 2.04E-27 2.04E-27 2.04E-27 2.04E-27 2.04E-27 2.04E-27 2.04E-27 2.04E-27 2.04E-27 2.04E-27 2.04E-27 2.04E-27 3.32E-10 2.03E-15 3.13E-23 1.36E-28 1.35E-28
Downregulated	JUG2 TTR TMSE44X DSP LCOR TTR CRVBA2 SLC30A8 MT1G NEFM GCG MT1X ACVR1C NPTX2 RP11-788H18.1 HADH RTN1 SMC2 ASPH EPHX1 PCDH7 EGFL7 TLE4 HPCA AIF1 TUB828 LBH SLC25A5 HMGB3 STMN2 ROB02 TNFRSF21 HNRNPA1 ALDH1A1 FTL CHODL NME1 ANGF72 PPP1R1A SURF4 SVIP FGF12 PLXNA2 RAN PCSK2 APOA2 SNH68 KRT19	0.51930402 0.5145366 0.50794817 0.50065824 -2.1840245 -2.0521569 -1.4277739 -1.3136923 -1.047069 -1.4277739 -1.3136923 -1.010624 -0.9259451 -0.016242 -0.828471 -0.016242 -0.828471 -0.016242 -0.8384374 -0.8384374 -0.8384374 -0.8384374 -0.8384374 -0.8384374 -0.8384374 -0.8384374 -0.775651 -0.775651 -0.775651 -0.6797651 -0.6797651 -0.67414 -0.6674345 -0.6674345 -0.6674345 -0.66343054 -0.6612025 -0.6343054 -0.6343054 -0.6343054 -0.6343054 -0.63927494 -0.6343054 -0.6343054 -0.6343054 -0.63927494 -0.6343054 -0.6343054 -0.6343054 -0.6343054 -0.6343054 -0.5321187 -0.5573655 -0.552311741 -0.552311741 -0.52831174 -0.5283	1.302-03 4.902-05 2.14E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 1.24E-10 2.25E-10 2.315E-22 2.315E-22 2.315E-22 2.315E-22 2.315E-22 2.315E-22 2.315E-22 2.315E-22 2.315E-10 2.32E-20 2.32E-10 2.32E-10 2.33E-10 2.33E-10 2.33E-10 2.33E-10 2.33E-22 2.33E-10 2.33E-22 2.3
Downregulated	JUG2 TTR TMSE44X DSP LCOR TTR CRYBA2 SUC30A8 MT1G NEFM GCG MT1X ACVR1C NPTX2 RP11-788H18.1 HADH RTM1 SMC2 ASPH EPHX1 P11-788H18.1 HADH RTM1 SMC2 ASPH EPHX1 PCDH7 EGFL7 TUE4 HPCA AIF1 TUB82B LBH PCDH7 EGFL7 TUE4 HPCA AIF1 TUB82B LBH SUC25A5 STMR2 ROB02 TTRFSF21 HNRNPA1 ALDH1A1 FTL CHODL NME1 ANGF12 PPP1R1A SURF4 SVIP FGF12 PLXNA2 RAN PCSK2 APOA2 SNH08 KRT19 MAN1A1	0.51930402 0.5145366 0.50794817 0.50065824 -2.1840245 -2.0521569 -1.4277739 -1.3136923 -1.7506659 -1.4277739 -1.3136923 -1.0106026 -1.010642 -0.9577836 -0.9577836 -0.9577836 -0.9577836 -0.9577836 -0.8849714 -0.8849714 -0.8849714 -0.8849714 -0.8849714 -0.8849714 -0.8849714 -0.8849714 -0.8849714 -0.8849714 -0.8849714 -0.8849714 -0.83531848 -0.83531848 -0.8161754 -0.775815 -0.7358968 -0.675164 -0.675104 -0.6712014 -0.6712014 -0.6712014 -0.6712014 -0.6543035 -0.6343054 -0.6343054 -0.5745254 -0.5745254 -0.5745254 -0.5745254 -0.5745254 -0.5745254 -0.5745254 -0.5745254 -0.5745254 -0.5745254 -0.5745254 -0.5745254 -0.5745254 -0.5745254 -0.5745254 -0.522466 -0.5224465 -0.5224465 -0.5224465 -0.5224465 -0.5224465 -0.5224455 -0.524455 -0.52455 -0.52	1.302-03 4.902-05 2.14E-10 1.24E-19 2.48E-52 4.99E-67 1.60E-42 0.0097721 1.40E-11 4.83E-36 0.03612605 1.102-46 1.55E-11 3.40E-12 3.15E-22 6.72E-34 2.72E-16 9.22E-20 8.25E-28 2.46E-17 1.78E-15 1.37E-15 3.32E-17 2.04E-27 2.46E-17 1.683E-20 8.25E-28 2.246E-17 1.683E-20 8.25E-28 2.246E-17 1.683E-20 8.32E-17 5.72E-39 3.32E-17 2.04E-27 2.04E-27 2.04E-27 2.04E-27 2.04E-27 2.04E-27 2.04E-27 2.04E-27 2.04E-27 2.05E-12 3.32E-17 2.04E-27 2.05E-12 3.32E-17 2.04E-27 2.05E-12 3.32E-17 2.04E-27 2.05E-12 3.32E-17 2.04E-27 2.05E-12 3.32E-17 2.04E-27 2.05E-12 3.32E-17 3.32E-10 3.32E-17 3.32E-10 3.32E-17 3.32E-10 3.32E-17 3.32E-10 3.32E-17 3.32E-10 3.32E-17 3.32E-10 3.32E-17 3.32E-10 3.32E-17 3.32E-10 3.32E-17 3.32E-10 3.32E-17 3.32E-10 3.32E-17 3.32E-10 3.32E-17 3.32E-10 3.32

Supplementary Table 8. Differentially Expressed genes from MAFB +/+ and -/- cells in GCG PPY PYY GAST high (Alpha-like) cells at D20 (P_adj<0.1, FC>0.5)

Uprogulated	anno	ava logEC	n val adi
opregulated	GAST	2.34845121	4.24E-33
	SST	1.87687227	6.10E-44
	APOC1	1.42598852	2.08E-34
	PPY	1.39317369	9.42E-10
	GHRL	1.20480579	2 275 28
	CALR2	1.19890362	3.37E-28 4 96F-12
	LY6E	1.02849752	9.55E-25
	TIMP3	0.97653856	6.30E-21
	VIM	0.94252217	2.57E-17
	FXYD2	0.90341815	7.48E-06
	MAFB	0.86993285	5.57E-33
	APOF	0.8087/6//	2 76F-25
	RGS4	0.80821309	5.77E-24
	ISG15	0.76157627	3.34E-21
	LYZ	0.75428174	0.01653335
	AMBP	0.75381568	1.68E-13
	HSPA1B	0.73811796	1.77E-22
	NEAT1	0.72203225	4.91E-07 7.69E-06
	PYY	0.6740438	1
	MLF1	0.67158036	3.98E-19
	FOXJ1	0.66121597	3.15E-06
	TMOD1	0.65144922	4.25E-22
	BAMBI	0.64792289	6.78E-17
	HSP90AA1	0.63034606	3.50E-29 8.24E-08
	TDO2	0.58867598	0.00101285
	PIFO	0.57029439	7.96E-13
	TMX4	0.5698137	7.19E-11
	HSPA1A	0.56574268	3.53E-10
	DSP	0.55331361	1.13E-15
	AGT	0.55011204	3.41E-19 1 97E-05
	GC	0.54338691	0.43178532
	MDK	0.54269379	4.40E-12
	SEZ6L	0.5424836	1.97E-19
	RPL17	0.53597572	6.38E-29
		0.5269/3	6.49E-16 3 75E-19
	MYH10	0.51451642	1.90E-17
	UBE2L6	0.514254	2.58E-18
	C8orf4	0.51300744	1.17E-07
	HEPACAM2	0.51253835	5.94E-12
	DNAJB1	0.51086168	3.59E-15
	EIF4A2	0.50786082	7.53E-26 8 17E-09
	351330	0.3010338	8.172-09
Downregulated	INS	-2.6998144	5.21E-122
	GCG	-2.3085079	3.86E-73
		-2.03669//	2.6/E-113 7.56E-31
	ACVR1C	-1.4741353	2.27E-72
	EPHX1	-1.0894711	9.60E-75
	TTR	-1.0717345	8.43E-31
	SLC30A8	-1.0484865	3.94E-49
	PPP1R1A	-0.8705498	3.16E-51
		-0.8705292	2.63E-31 3.10E-23
	GAL	-0.8321412	3.24E-07
	PCSK2	-0.8142138	4.87E-39
	RP11-788H18	-0.7751951	2.08E-30
	STMN2	-0.6887093	2.25E-24
		-U.6817355	3.21E-35
	SERPINI1	-0.6313049	2.37E-43 7.91E-23
	MAN1A1	-0.5520895	2.80E-16
	C2CD4A	-0.5212733	4.15E-19
	MT-ATP6	-0.5107123	4.85E-24
	NPTX2	-0.5058441	7.00E-27

Supplementary Table 9. Differentially Expressed genes from MAFB +/+ and -/- cells in SST HHEX high (Delta-like) cells at D20 (P_adj<0.1, FC>0.5)

Upregulated	Gene	avg_logFC	p_val_adj
	PPY	1.16921263	0.00065802
	TPPP3	0.94230623	4.95E-05
	SST	0.83167127	3.23E-07
	APOC1	0.7776412	0.00014862
	MAFB	0.71361123	2.97E-07
	APOE	0.70040977	1.17E-05
	LY6E	0.6953392	0.00016574
	ISG15	0.69312906	2.74E-05
	ΡΥΥ	0.6342115	0.00345824
	C1orf192	0.56016347	0.01327972
	IFI6	0.55576006	1.14E-11
Downregulated	INS	-2.8150699	3.58E-59
	CRYBA2	-2.2224018	4.01E-55
	ACVR1C	-1.3812356	3.03E-35
	GCG	-1.143319	4.24E-46
	TTR	-1.1143138	5.29E-20
	EPHX1	-1.0512858	5.57E-33
	PPP1R1A	-1.024554	1.87E-36
	MT1X	-0.9083369	0.00957171
	HADH	-0.8972487	2.75E-21
	STMN2	-0.8549379	5.11E-12
	MAN1A1	-0.8211267	3.64E-19
	NEUROD1	-0.8039444	1.83E-12
	FABP5	-0.7611367	1.93E-13
	IGFBP5	-0.7404403	7.73E-05
	KRT19	-0.7397835	2.47E-09
	HMGB3	-0.7186303	1.31E-11
	ERO1LB	-0.7150173	1.94E-09
	C9orf16	-0.6663357	7.60E-09
	MT-ATP6	-0.6039107	7.24E-15
	PCSK2	-0.5968298	1.43E-09
	SLC30A8	-0.5885128	4.54E-05
	PLCE1	-0.5561556	2.75E-11
	FTL	-0.5540723	2.65E-10
	AIF1	-0.5484026	4.55E-08
	MT-ND2	-0.5467455	3.56E-13
	TUBB2B	-0.5396288	1.38E-05
	RPS21	-0.5078175	6.78E-12
	SNORA76	-0.5072658	2.52E-07
	IGFBP2	-0.5026126	0.0011693
	SLC7A8	-0.5016193	6.41E-07

Day	Media	Supplemen	t				
	Seed hESCs 5.5 million cells/ well in 6 well plates with D0 media						
D0	Day 0		HERβ1	Activin A	FGF-2		
	Day 0		10ng/ml	10ng/ml	4.16ng/ml		
D1	Rinse cells with DPBS (w/o Ca ²⁺ , Mg ²⁺) for 5 min and added Day 1 diff media						
			FBS	Activin A	ITS	Wnt-3a	
	Day 1		0.2%	100ng/ml	0.02X	50ng/ml	
<u>ר</u> ח			FBS	Activin A	ITS		
Dz	Day Z	Day Z		100ng/ml	0.05X		
2			FBS	KGF	ITS	TGF-β IV	
D3	Day 5		0.2%	25ng/ml	0.1X	2.5µM	
D4-5	Day 4-5		FBS	KGF	ITS		
D4-3	Day 4-5		0.2%	25ng/ml	0.1X		
D6-8	Day 6-8	Day 6.8		TTNPB			
D0-0	Day 0-0		100 ng/ml	3nM			
₽0_11	Day 9-11		Noggin	Alk5i II	DAPT		
D9-11	Day 9-11		50 ng/ml	1µM	1µM		
D12-18	Dav12-18		Alk5i II				
D12-10	Day 12-10		1µM				
D19-onward	Day 19		Day 19 me	dia on ward	until ~ day 55	5	

Supplementary Table 10. hESC differentiation into α -like cells – Media components

Day	Media comp	onents				
D0	DMEM/F-12	1xGlutamax	1xMEM-NEAA	1x 2-Mercap	otoethanol	4% KSR
D1-5	RPMI	1xGlutamax				
D6-8	DMEM	1xGlutamax				
D9-11	DMEM/F-12	1xGlutamax	1xMEM-NEAA	1xB27		
D11-54	DMEM/F-12	1xGlutamax	1xMEM_NEAA	1xB27	0.2%BSA	

Supplementary Table 11. hESC differentiation into α-like cells – Backbone Media Formulation

Supplementary Table 12. Chemicals and media components

Components	Vendor	Cat. No.	
DMEM	Life Tech	11960-051	
DMEM-F12	Life Tech	11320-033	
RPMI	Mediatech	15-040-CM	
HERβ1(Heregulin-β1)	PeproTech	100-03	
Activin A	R&D	338-AC/CF	
FGF-2	R&D	233-FB/CF	
FBS	Corning	35-011-CV	
ITS (Insulin-Transferrin-Selenium)	Gibco	41400045	
Wnt-3a	R&D	5036-WN-010/CF	
TGF- β IV (TGF- β RI Kinase Inhibitor IV)	CalBiochem	616454-2MG	
KGF (FGF-7)	R&D	251-KG-050/CF	
Noggin	R&D	3344-NG	
ТТЛРВ	Sigma-Aldrich	T3757-10MG	
Alk5i II (ALK5 Inhibitor 2)	Axxora	ALX-270-445-M001	
DAPT	Sigma-Aldrich	D5942-5MG	
Glutamax	Gibco	35050-061	
MEM-NEAA	Gibco	11140-050	
2-Mercaptoethanol	Emd-Millipore	ES-007-E	
KSR (KnockOut [™] Serum replacement)	Gibco	10828-028	
B27 (NeuroCult [™] SM1 Neuronal)	Stemcell Technologies	5711	
BSA	Sigma-Aldrich	A4503-50G	
Doxycycline	Sigma-Aldrich	D9891	
LDN	Fisher	04-0074-10	

Supplementary Table 13. CRISPR gRNA target sequences for targeting AAVS1 locus

Primer	Sequence (5'to 3')
AAVS1-cr1-ex	GATGACCGAGTACAAGCCCA
AAVS1-cr2-ex	GACAGTACTAAGCTTTACTA

Supplementary Table 14. Antibodies used for FACS analysis

Manufacturer	Antibody	Catalogue No.	Dilution	Fluorophore
BD Pharmingen/Fisher	Foxa2	561589	1:100	PE
BD Pharmingen/Fisher	Sox17	562205	1:100	Alexa F. 488
Biolegend	TRA-1-60-R	330605	1:200	Alexa F. 647
BD Pharmingen/Fisher	PDX1	562161	1:50	PE
BD Pharmingen/Fisher	NKX6.1	563338	1:50	Alexa F. 647
BD Pharmingen/Fisher	C-peptide	051109MI	1:200	Alexa F. 488
Fisher	PAX6	562249	1:50	Alexa F. 647
BD Pharmingen/Fisher	NKX2.2	564730	1:50	PE
BD Pharmingen/Fisher	Chromogranin A	BDB564563	1:50	PE
Sigma	Glucagon	G2654	1:1000	Alexa F. 647
BD Pharmingen/Fisher	KI67	550609	1:20	Alexa F. 647
Millipore	ARX	MABN102	1:200	PE
DAKO	SST	A0566	1:250	Alexa F. 568
Peninsula Laboratories International, Inc.	PPY	T-4088	1:500	Alexa F. 647

Supplementary Table 15. Antibodies used for IF analysis

Antibody	Species	IF Dilution	Company	Catalogue No.
Somatostatin	Rabbit	1:250	DAKO	A0566
Somatostatin	Sheep	1:250	Biogenesis	8330-0350
PDX1	Goat	1:100	R&D	AF2419
NKX6.1	Mouse	1:100	Hybridoma Bank, U Iowa	F55A10-c
Sox17	Goat	1:200	R&D	AF1924
FoxA2	Rabbit	1:1000	Millipore	07-633
KI-67	Mouse	1:400	BD	550609
NGN3	Sheep	1:200	R&D	AF3444
Glucagon	Rabbit	1:200	Linco	4030-01F
Glucagon	Mouse	1:250	Sigma	G2654
C-peptide	Rat	1:1000	DSHB	GN-1D4-C
NGN3	Sheep	1:200	R&D	AF3444
ARX	Mouse	1:200	Millipore	MABN102
HHEX	Rabbit	1:200	R&D	MAB83771-100
PPY	Rabbit	1:2000	Peninsula Laboratories International, Inc.	T-4088
MAFB	Rabbit	1:250	Sigma	HPA005653

Antibody	Species	IF Dilution	Company	Catalogue No.
GAPDH	Mouse	1:3000	Santa Cruz	sc-32233
MAFB	Rabbit	1:300	Sigma	HPA0055653
Somatostatin	Rabbit	1:2000	Dako	A0566
Vinculin	Mouse	1:10,000	Santa Cruz	sc-73614

Supplementary Table 16. Antibodies used for WB analysis

Supplementary Table 17. qPCR primer sequences

Primer Name	Forward Sequence	Reverse Sequence
ALDH1A3	TCTGAGGGTTCTAATACAGCCC	CCCTGGAGACGATGGATACAG
ARX	GTGCAAGGCTCCCCTAAGAG	CGTTCTCGCGGTACGACTT
CHGA	TGACCTCAACGATGCATTTC	CTGTCCTGGCTCTTCTGCTC
GAPDH	CTCACCGGATGCACCAATGTT	CGCGTTGCTCACAATGTTCAT
GCG	GAGATTTCCCAGAAGAGGTCG	TGGCGGCAAGATTATCAAGAA
GHRL	CAACGCCCCCTTTGATGTTG	CTGCTGGTACTGAACCCCTG
HHEX	GCGAGAGACAGGTCAAAACC	AGGGCGAACATTGAGAGCTA
HNF6	ATGTCCAGCGTCGAACTCTAC	TGCTTTGGTACAAGTGCTTGAT
INS	AGAGGCCATCAAGCAGATCACTGT	ACAGGTGTTGGTTCACAAAGGCTG
MAFA	GAGAGCGAGAAGTGCCAACT	TTCTCCTTGTACAGGTCCCG
MAFB	CATAGAGAACGTGGCAGCAA	ATGCCCGGAACTTTTTCTTT
NEUROD1	ATGACCAAATCGTACAGCGAG	GTTCATGGCTTCGAGGTCGT
NGN3	TAAGAGCGAGTTGGCACTGAGCAA	TTTGAGTCAGCGCCCAGATGTAGT
NKX2.2	GGAGCTTGAGTCCTGAGGG	TCTACGACAGCAGCGACAAC
NKX6.1	CCGAGTCCTGCTTCTTCTTG	ATTCGTTGGGGATGACAGAG
PAX4	CTACCGCACAGGTGTCTTGG	CGTTGGATTTCCCAGGCAA
PAX6	TGGGCAGGTATTACGAGACTG	ACTCCCGCTTATACTGGGCTA
PDX1	TACTGGATTGGCGTTGTTTGTGGC	AGGGAGCCTTCCAATGTGTATGGT
PPY	AGTGTACCCAGGGGACAATGC	CAGCATGTTGAGTGTATCTACGGA
Pre-INS	GTGAACCAACACCTGTGCGG	AGGGGCAGCAATGGGCAGTT
PTF1A	TTCACCGACCAGTCTTCACG	GTGGCTAAGGAACTCCACCT
SOX9	AGCGAACGCACATCAAGAC	CTGTAGGCGATCTGTTGGGG
SST	CGCTGTCCATGGTCCTG	GGGCATCATTCTCCGTCT