Electronic Supplementary Material

Isolation and culture of porcine neonatal islet cell clusters

Freshly isolated NICCs were cultured in petri dishes containing maintenance medium (1:1 mixture of Ham's F12 and medium 199) containing (in mmol/l): 10 glucose, 10 L-glutamine, 0.5 Pefabloc, 10 HEPES, 10 nicotinamide, 0.5% BSA, 0.062% glutathione, 100 U/ml penicillin, and 0.1 mg/ml streptomycin, 2.5 µg/ml amphotericin, 25 U/ml heparin, 100 KIU aprotinin, 10 µmol/l TroloxTM, 1x BME vitamins, 15.2 µmol/l zinc sulphate and 1 µmol/l liraglutide. Since FCS contains high amounts of fetuin-A, NICCs maturation was conducted in FCS-free medium. At culture day 5, NICCs were placed in FCS-free Ham's F10 maturation medium containing 10 mmol/l glucose, 50 µmol/l isobutylmethylxanthine, 2 mmol/l L-glutamine, 10 mmol/l nicotinamide, 1.25 mmol/l CaCl2, 100 U/ml penicillin, 0.1 mg/ml streptomycin and supplemented with 0.6 mg/ml human serum albumin (HSA).

Isolated human islets

The isolated human islets were cultured overnight in CMRL1066 medium supplemented with (in mmol/l): 5 glucose, 2 L-glutamine, 10 HEPES, and 10% FCS.

Transcriptome analysis

The mRNA samples were then subjected to the workflow for strand specific RNAseq library preparation (Ultra Directional RNA Library Prep II, NEB). Following ligation, adapters were depleted by 1X XP bead purification. Indexing was carried out during the following PCR enrichment (15 cycles, 65 °C). The libraries were quantified using Qubit dsDNA HS Assay Kit (Invitrogen) and used for 75bp single read sequencing on Illumina NextSeq 500, resulting in an average of 28 Mio sequenced fragments per sample. For the bioinformatics analysis, the workflow nf-core/rnaseq (https://nf-co.re/rnaseq, release 1.2) was set-up as following: FASTQC was used to determine the quality of the FASTQ files; adapter and quality-based trimming were subsequently performed with Trim Galore; STAR aligner (v2.6.1) was used to

map the quality controlled reads to the pig genome (Ensembl release 94). Read counting on the features was performed with feature counts. MultiQC (v1.6) was used to aggregate the final results into one html report. For differential expression analysis, the row read count table resulting from the nf-core/rnaseq workflow was processed with the R package DESeq2 v1.22.1.

Western blotting

NICCs and human islets were lysed in RIPA buffer containing (mmol/l): 25 Tris/HCl (pH 7.5), 150 NaCl, 2 EDTA, 10 NaF, 1 Na3VO4, 10% glycerol, 1% Nonidet-P40, 0.1% SDS, 0.1% C24H39NaO4 and protease inhibitors.

ESM Table 1 Reagents and Resources.

ESM Table 2 Human islets checklist: characteristics of the isolated human islets and islets donors.

ESM Table 3 Characteristics of the human donors of pancreatic resections.

ESM Table 4 Differentially expressed genes in NICCs following in vitro maturation. RNA sequencing results showing all genes with a significantly altered expression level (base Mean >50; -1>log2FC>1; p adjusted < 0.05) in NICCs maturated in standard medium (HSA/d5 versus HSA/d1).

ESM Table 5 Differentially expressed genes in NICCs isolated from 4 days old animals upon culture the presence of fetuin-A. RNA sequencing results showing all genes with a significantly altered expression level (base Mean > 50; -1>log2FC>1; p adjusted < 0.05) in NICCs isolated from 4d old animals and cultured in medium with fetuin-A (Fetuin-A/d5 versus HSA/d5).

ESM Table 6 Differentially expressed genes in NICCs isolated from 4 days old animals following in vitro maturation in the presence of TGFBRI inhibitor SB431542. RNA sequencing results showing all genes with a significantly altered expression level (base mean

>50, -1>log2FC>1; p adjusted < 0.05) in 4 days old NICCs maturated in the presence of SB431542 (HSA + SB/d5 versus HSA/d5).

ESM Table 1

REAGENT or RESOURCE	REFRENCE OR SOURCE	IDENTIFIER
Antibodies		
ALDOB	ProteinTech Group, Manchester, UK	18065-1-AP
SMAD2/3	Cell Signaling Technology, Massachusetts, USA	5678
P-SMAD2 (Ser465/467) / P-SAMD3 (Ser423/425)	Cell Signaling Technology	8828
PDX1	Abcam, Cambridge, UK	47383
P16/Ink4a	Santa Cruz Biotechnology, Texas, USA	1661
cMYC	Cell Signaling Technology	5605
Ki67	Abcam	15580
Insulin	Abcam	8304
Insulin	Dako Agilent, CA, USA	A0564
GAPDH	Cell Signaling Technology	2118
Tubulin	Cell Signaling Technology	2148
Goat anti-Mouse IgG Secondary Antibody, Alexa Fluor 488	Thermo Fischer Scientific, Massachusetts, USA	A28175
Goat anti-rabbit IgG Secondary Antibody, Alexa Fluor 488	Thermo Fischer Scientific	A11008
Goat anti-Rabbit IgG Secondary Antibody, Alexa Fluor 546	Thermo Fischer Scientific	A11035
Opti-View DAB IHC detection	Roche, Switzerland	760-700
Horse radish peroxidase-coupled secondary antibody	GE Healthcare, Germany	NA934
Chemicals, Peptides, and Recombinant Proteins		
Fetuin-A (α2-hs-Glycoprotein from human plasma)	Sigma Aldrich, Missouri, USA	G0516
Human Serum Abumin 20% (HSA)	CSL Behring, Marburg, Germany	
Bovine Serum Albumin (BSA- fraction V)	Sigma Aldrich	A3294
Forskolin	Sigma Aldrich	F6886
DAPI	Sigma Aldrich	D9542
TOPRO3	Invitrogen	N1
SB431542	Merck Millipore, Massachusetts, USA	566405
Palmitic acid	Sigma Aldrich	P0500

CLI-095	InvivoGen, California, USA	Tlrl-cli95
Human TGFβ-1	R&D Systems, Minnesota, USA	100-B
Human Recombinant Prolactin	R&D Systems	682-PL
Collagenase V	Sigma Aldrich	C9263
Illumina NextSeq 500	Illumina, California, USA	
Porcine Insulin ELISA	Mercodia, Uppsala, Sweden	10-1200-01
Transcriptor First Strand kit	Roche, Basel, Switzerland	04379012001
Human TGFβ-1 ELISA	R&D Systems	DB100B
Deposited Data	RNAseq Data	GEO: GSE144950
Oligonucleotides		
Sus Scrofa		
INS F 5'-GTGGCATCGTGGAGCAGT-3' R 5'-CGGCCTAGTTGCAGTAGTTCTC-3'		
PDX1 F 5'-TGTGGTTTCCAGATTGCTTG-3' R 5'-TCCACAAGCATCACCTGAAC-3'		
MAFA F 5'-TGCCAGAAAGAGCCAAGAA-3' R 5'-GTAGGAGGTGGCGTCGTG-3'		
NEUROD1 F 5'-AAGCCATGAATGCGGAAG-3' R 5'-TCCTCTTCCAAGTCCTCGTC-3'		
CDKN2A F 5'-CACTTTGGTGGTCCTGCAC-3' R 5'-CCCTCTCCTCAGCCAGGT-3'		
SMAD7 F 5'-TCAGTGCCACCAAACACAGT-3' R 5'-GCTACGATGACCCCAAGGT-3'		
PRLR F 5'-TCCTACCAACTACACGCTGACTT-3' R 5'-GTCTGGACATTCATGGGTGA-3'		
FOXM1 F 5'-TCAAGACACCCGTTAAGGAGA-3' R 5'-ATGGGGAGGACAGATTTGCT-3'		
CCNB1 F 5'-GGCTCTTCTTGTTTTATGTACTTGG-3' R 5'-CAAGATGACTGAGCTTACATACAGTG-3'		
CENPA F 5'-TGACCAGACAACGTGCATCT-3' R 5'-TCATCTGGTCTTTGTGAAGTGG-3'		
CDK1 F 5'-GACGCTGACGTGGTAGCC-3' R 5'-GGATGTGGTAGATCCCAGCTTA-3'		
TOP2A F 5'-TCCACTGAGTGTACGCTTATCC-3' R 5'-GGCCTGAAACTGCCAAAGT-3'		

ABCC8 F 5’-TACGCCATGGTGTTCACAGT-3’ R 5’-AGACGTGACAAGGCACAGC-3’		
G6PC2 F 5’-TCATGTGTCTGGTATGTCATGG-3’ R 5’-ATCCATCCACCTGATGGTGT-3’		
UCN3 F 5’-TCACAGGCATTTCCACGAT-3’ R 5’-GGGCTGCAATCAGCATCT-3’		
GJD2 F 5’-CACTGCAGCTCGATCCAAG-3’ R 5’-TGGATAATGTAGAAGCGGGAGA-3’		
PCSK1 F 5’-ACCCTACCTCATGGCAACAG-3’ R 5’-TTCAAGACTGGCTGGGTAGC-3’		
SNAI1 F 5’-ACTTGTTGAGGGCCCAAGT-3’ R 5’-CAGAAATAGTTCCGGGAGACA-3’		
GCK F 5’-CTGGCTGCAGTACAGATGCT-3’ R 5’-CTTTTCCTTCTTGGCGCTCT-3’		
SYT4 F 5’-ATTGCGTCAATTCGGGTTT-3’ R 5’-TGTTCCTGTTTTGGCTCTTCA-3’		
SYT7 F 5’-GGCGTCCGGACACTACAG-3’ R 5’-CCCATCGGGAATGGAACT-3’		
IL1B F 5’-GGCAGATGGTGTCTGTCATC-3’ R 5’-CCTGGGAGGAGGGATTCTT-3’		
RBP3L F 5’-GAAAATGTACCAAGTGCCAGAA-3’ R 5’-TGTAGCACCTAAAACATTCTGGTTAG-3’		
Homo Sapiens		
FOXM1 F 5’-ACTTTAAGCACATTGCCAAGC-3’ R 5’-CGTGCAGGGAAAGGTTGT-3’		
PRLR F 5’-CCAGCGACCTTCATTCAGATA-3’ R 5’-GCCACTGCCCAGACAATAAT-3’		
TMEM27 F 5’-TTGTGGTTACAGACCCTTCAAA-3’ R 5’-GCATTGTTGATCCGGTTCTT-3’		
G6PC2 F 5’-TGTCTGTGGGATGGATAAGTTCT-3’ R 5’-GCCTGGAGTGTGTTCAAAGG-3’		
SLC30A8 F 5’-AGTAATTCTCTCAGCTCATGTTGC-3’ R 5’-GCAATTTCTCTCCGAACCAC-3’		
PCSK1 F 5’-CGGGGTTGGAGTTGCATA-3’ R 5’-CCTCAATAGCATCCGTCACA-3’		

UCN3 F 5'-ACAAGTTCATGGGGACGTG-3' R 5'-CGGCATCAGCATCTCTCC-3'		
Software		
Image Lab 5.2.1	BioRad Laboratories, Feldkirchen, Germany	
Graph Pad 8.4.0	NA	
Ingenuity Pathway Analysis Software https://analysis.ingenuity.com/pa/	Qiagen, Hilden Germany	
R package DESeq2 v1.22.1	NA	

ESM Table 2

Islet preparation	1	2	3	4	5	6	8	9
Unique Identifier	HP1012	H1267	H993	HP1354	HI9	HI1326	HI1332	HI1333
Donor Age (years)	55	54	63	58	59	63	62	54
Donor sex (M/F)	M	M	M	M	F	F	F	M
Donor BMI (kg/m2)	23.5	26.5	25.9	27.2	23.7	21.8	29.3	24.2
Source of islets	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT
Isolation center	Lille	Milano	Lille	Milano	Geneva	Milano	Milano	Milano
Donor's history of diabetes	no	no	no	no	no	no	no	no
Purity (%)	90	75	80	80	84	85	90	90
Viability (%)	95	95	98	90	90	95	95	95
Total culture time (d)	8	6	6	7	8	5	6	6

ESM Table 3. Charactersitics of the donors of human pancreatic resections

Donor identifier	SEX	AGE years	BMI	Fasting glucose mg/dl	Fasting insulin pmol/l	HbA1c %	Plasma fetuin-A µg/ml	Beta cell area % islet area	
P1	f	57	29.7	78	84	5.6	555.90	68.38	ND
P2	f	79	27.1	66	15	4.7	680.60	31.85	ND
P3	1	74	25.0	83	68	5.2	245.99	67.80	ND
P4	f	63	22.0	85	90	4.7	592.66	52.86	ND
P5	m	54	27.8	98	110	5.1	537.51	57.45	ND
P6	m	33	24.2	100	62	4.8	408.16	46.80	ND
P7	m	68	27.5	93	105	5.5	421.08	64.57	ND
P8	f	77	29.0	89	61	5.4	428.73	61.93	ND
P9	f	72	29.1	80	35	4.9	462.99	31.18	ND
P10	m	49	31.1	97	51	5.1	500.90	41.82	ND
P11	m	46	26.1	93	48	5.2	567.10	64.85	ND
P12	m	75	23.9	89	55	5.2	498.76	52.42	ND
P13	m	59	25.6	72	19	5.5	467.58	65.75	ND
P14	m	36	26.6	82	155	5.6	439.88	71.53	ND
P15	f	84	22.0	77	23	4.6	296.74	56.00	ND
P16	m	65	---	88	60	5.5	304.91	66.81	ND
P17	m	63	23.5	95	102	5.5	442.44	56.41	ND
P18	m	59	24.1	100	80	5.1	646.60	29.23	ND
P19	f	58	20.3	74	24	5.1	285.56	60.53	ND
P20	f	52	23.2	85	48	5.5	431.38	68.67	ND
P21	f	37	21.0	88	39	5.5	356.96	61.69	ND
P22	f	72	19.5	96	41	5.6	435.15	60.62	ND
P23	f	54	22.5	105	67	5.2	432.96	65.30	IFG
P24	f	66	24.2	113	47	5.6	251.02	50.36	IFG
P25	m	60	27.9	122	95	5.5	664.16	69.93	IFG
P26	m	55	25.9	107	128	5.3	546.05	65.47	IFG
P27	m	70	23.7	102	51	5.5	612.03	51.16	IFG
P28	m	61	25.3	117	72	5.9	202.48	46.43	IGT
P29	m	64	24.8	125	43	5.0	328.33	44.79	IFG
P30	m	76	25.0	107	88	6.4	385.66	66.57	IGT
P31	m	64	25.8	103	70	6.4	338.34	65.89	IGT
P32	m	49	23.5	104	64	5.7	496.53	43.73	IGT
P33	f	76	16.9	106	45	5.9	380.57	36.26	IGT
P34	m	50	21.0	102	34	5.3	605.33	65.15	IFG
P35	m	66	24.8	115	46	6.1	329.79	64.61	IGT
P36	m	56	19.5	102	25	6.1	300.95	50.20	IGT
P37	f	62	38.2	121	62	5.9	386.72	25.98	IGT
P38	m	77	26.5	77	18	5.9	331.92	34.47	IGT
P39	f	49	25.9	93	39	5.8	494.29	43.56	IGT
P40	f	56	19.8	117	24	6.2	449.74	56.74	IGT
P41	m	51	24.7	110	54	5.6	358.99	66.58	IFG
P42	m	58	29.4	102	97	5.8	808.88	48.03	IGT
P43	f	76	32.9	124	135	5.6	466.33	72.39	IFG
P44	m	79	25.7	81	13	6.3	298.61	58.30	IGT
P45	f	66	20.1	112	30	6.1	471.18	68.80	IGT
P46	m	76	24.8	93	42	5.9	415.99	61.00	IGT
P47	m	87	25.8	106	43	5.2	212.48	57.49	IFG
P48	m	51	18.5	102	8	5.3	75.16	60.71	IFG
P49	m	75	29.3	101	150	5.4	755.95	61.23	IFG
P50	f	62	24.2	102	38	6.0	310.47	51.66	IGT
P51	f	63	21.6	109	52	6.1	443.02	67.05	IGT
P52	f	75	24.5	81	82	6.0	473.62	54.26	IGT
P53	m	67	28.7	94	148	6.0	347.16	52.81	IGT
P54	f	74	22.1	116	67	5.9	626.16	47.77	IGT
P55	m	49	21.4	116	108	6.7	323.64	61.10	T2DM

P56	f	61	25.2	107	22	6.5	310.19	44.97	T2DM
P57	m	78	21.0	115	29	4.6	633.13	35.48	T2DM
P58	m	69	30.3	362	76	9.4	592.89	56.38	T2DM
P59	m	64	42.4	156	271	6.6	593.10	64.35	T2DM
P60	f	59	23.6	126	73	6.9	523.92	55.86	T2DM
P61	f	70	---	366	1056	12.6	358.38	61.78	T2DM
P62	m	75	22.6	135	97	6.0	376.34	58.29	T2DM
P63	f	45	24.5	142	77	7.0	740.06	63.54	T2DM
P64	m	64	23.7	179	91	8.5	447.64	62.34	T2DM
P65	f	77	18.8	148	32	6.8	411.49	62.91	T2DM
P66	m	79	22.3	92	19	6.5	330.87	59.39	T2DM
P67	m	55	23.0	111	59	6.9	582.79	57.08	T2DM
P68	f	75	24.0	163	110	7.9	484.98	58.65	T2DM
P69	f	70	26.6	181	42	7.3	450.59	61.92	T2DM
P70	m	63	25.3	128	93	5.6	286.24	70.55	T2DM
P71	f	76	29.6	98	92	6.8	367.59	52.92	T2DM
P72	f	71	28.0	124	35	7.4	653.89	35.20	T2DM
P73	m	75	23.2	---	---	7.2	593.81	46.03	T2DM
P74	m	76	24.0	130	53	5.2	862.65	67.20	T2DM
P75	f	75	23.8	144	59	8.0	384.81	54.34	T2DM
P76	m	66	26.1	105	127	7.9	655.35	48.68	T2DM
P77	m	77	31.1	136	55	6.3	525.58	45.95	T2DM
P78	m	79	28.1	---	58	8.3	349.38	56.28	T2DM

ESM Table 4: DEGs in NICCs follwing in vitro maturation

Gene	Base Mean	log2FC	p adjusted	Gene	Base Mean	log2FC	p adjusted	Gene	Base Mean	log2FC	p adjusted
GCG	277078	2.05	0.000210743	BAALC	560	1.00	0.00888218	ADGRV1	147	1.77	9.55E-09
CHGA	83091	2.75	7.50E-10	SLC7A14	556	1.46	0.00478387	NEURL1B	144	1.03	0.047226219
INS	43067	1.61	0.032114945	KCNH6	551	1.36	0.0059594	SULT4A1	144	1.04	4.09E-06
SST	36849	1.71	1.01E-06	IRX2	540	1.41	0.00036019	B3GALT5	143	1.63	4.90E-15
CFD	21617	1.14	0.002950341	CLDN2	538	-2.36	9.12E-05	SNAP91	142	1.22	3.33E-05
COL1A1	21532	-1.53	0.015525605	FBXL16	530	1.02	1.22E-06	STEAP2	141	1.35	0.000158284
RPS12	20939	-1.00	1.57E-14	MAPK8IP2	527	1.32	6.33E-05	HCN4	137	1.71	4.00E-05
CHGB	20938	1.62	0.002966271	PLEKHS1	523	2.68	0.00429352	FAM184A	137	1.62	1.14E-06
PCSK1	14037	1.56	0.027312825	NRCAM	523	1.29	1.34E-12	RCVRN	136	1.30	0.001121921
CPE	13424	2.49	2.84E-08	SLC25A53	518	1.13	0.03973873	CBLN4	136	2.65	0.000355491
CRTAC1	12909	1.47	9.05E-06	HSD17B13	511	-1.05	0.00015562	ST8SIA3	136	1.29	0.000852214
YBX3	11917	-1.03	6.21E-05	HSD17B13	511	-1.05	0.00015562	CNTN4	132	1.39	0.000775174
PCSK2	11191	2.11	5.61E-05	ANK2	507	1.05	0.00526573	LTC4S	132	-1.81	0.02462859
PPY	10557	1.75	0.000300393	ST18	501	1.31	0.00301927	PKHD1L1	132	1.79	5.74E-08
S100A6	10491	-1.21	1.46E-05	MGAM	500	1.45	0.0007209	FAM3B	131	1.07	0.001008665
SCG2	9725	1.88	0.000967341	RAB9B	489	1.29	0.01000654	ASTN2	131	1.03	0.011149458
PAPPA2	8577	2.95	2.79E-06	PLCG2	479	1.26	5.74E-08	BEX5	130	1.48	0.001384154
SCGN	8275	1.68	0.000821926	C3orf70	477	1.12	0.00036019	IGFBPL1	130	1.66	0.001893839
SCG5	8234	2.03	8.25E-10	PAPLN	468	1.49	3.30E-10	REG4	129	2.52	0.043724759
CLPS	7440	-3.77	1.87E-09	SNAI2	466	-1.57	2.62E-06	TMEM151A	127	1.06	0.00015436
TIMP1	6503	-1.77	7.43E-08	GPX3	458	1.52	0.00527801	TLCD2	126	1.03	9.25E-13
VGF	5959	1.40	0.003512179	ANG	458	-1.80	0.02505642	GRIK4	126	1.46	0.00322882
BTG2	5771	-1.57	1.62E-13	PNLIPRP1	458	-1.65	0.00100117	ABHD15	125	1.46	0.000140924
PRSS2	5768	3.62	0.000601572	ASB9	457	1.28	0.03924073	LEPR	124	1.90	1.49E-06
SLC7A8	5724	1.09	0.005982663	CRMP1	455	1.10	1.15E-05	NEUROG3	124	1.10	0.000586464
MMP9	5434	1.97	4.80E-13	RBP4	450	1.60	0.00067418	BMP3	123	1.12	0.000240169
PDCD4	5365	-1.08	0.014699279	GLYCTK	450	1.07	1.00E-06	FAS	123	-1.09	1.63E-07
SLC7A2	5273	1.35	0.002982104	PKNOX2	446	-1.37	0.00028101	CCDC60	123	1.58	0.000597552
HEPACAM2	5190	1.55	0.004663801	ACE	440	1.47	1.09E-10	CCDC60	123	1.58	0.000597552
APOA1	4856	1.44	5.74E-08	SEL1L3	437	1.14	0.0001867	AATK	123	1.58	0.000210743
ANKRD1	4729	1.59	0.017244845	RNASE4	427	-1.18	0.03114847	ASPN	122	-1.85	0.031811515
TNC	4663	-2.25	0.000568952	PPP1R1A	420	2.16	7.78E-08	SLC24A2	120	3.19	0.000597552
GRIA3	4295	1.79	6.38E-07	TSPAN11	416	1.35	0.00071252	DPYSL4	120	1.06	1.11E-06
TTR	4028	1.76	6.72E-05	RADX	413	1.52	0.00010081	ACTG2	118	-2.36	0.001589912
CPLX2	3963	1.29	0.000160145	SCN3A	411	1.28	1.84E-05	ADGRB3	117	1.13	0.001116713
CACNA2D1	3945	1.26	9.61E-06	MMP17	411	2.08	2.73E-05	PRODH2	116	2.22	3.72E-12
TF	3886	4.06	3.97E-14	CACNA1C	406	1.06	0.00544477	C1QB	116	1.54	0.000817443
PTPRN	3830	1.81	7.77E-06	C4BPA	399	1.39	0.00012901	HPX	115	2.14	1.20E-07
CNTN1	3702	2.04	4.05E-06	C4BPA	399	1.39	0.00012901	USP35	115	1.02	5.68E-07
SCG3	3684	1.40	3.68E-05	SLC4A10	393	1.59	0.00073339	FRRS1L	115	1.80	3.43E-05
LRRN3	3662	1.57	0.024988661	RPS6KL1	393	1.15	3.80E-26	TRPC5	115	1.16	0.018587034
CBX6	3646	1.01	0.000415972	CERKL	392	1.37	0.00078517	ASTN1	114	1.19	5.17E-05
ABCC8	3418	1.78	0.001838096	NELL2	391	1.38	0.00087423	ZNF536	113	1.07	0.026207544
BHLHE40	3357	-1.16	1.14E-07	PBK	387	1.31	0.02646044	NMB	113	-1.98	1.88E-06
PTPRN2	3355	2.07	5.09E-07	SLC4A8	384	1.46	1.40E-06	GLP1R	113	1.01	0.001939944
TSC22D3	3285	-1.10	0.009104797	NFASC	382	1.75	5.91E-08	DAB1	112	1.38	1.79E-05
LBH	3248	-1.04	0.002041128	SEMA3E	378	1.23	2.51E-07	RF00002	111	-1.30	4.24E-06

GPNMB	3227	1.50	3.05E-07	MGAT3	377	1.08	2.37E-06	TFF3	110	1.81	0.035340147
DDIT4	3111	-1.47	9.47E-18	CAMK2B	376	1.19	0.00038109	FXYD1	110	1.37	9.54E-05
C14orf132	3099	1.03	6.04E-05	ITGA4	376	1.44	0.00369191	CAPN6	110	2.48	0.031299357
MT1A	3004	-2.72	0.001220079	SLC25A34	375	1.11	1.14E-07	ZNF483	109	1.02	1.56E-09
MT1A	3004	-2.72	0.001220079	PLCL2	373	1.36	0.00722632	THSD4	109	1.44	1.86E-07
ABCA1	2999	1.64	3.95E-18	TNR	371	2.56	1.53E-15	RNF152	109	1.05	0.000574929
PAX6	2938	1.24	0.003781555	CABP7	368	1.84	5.17E-10	SRPX2	108	-1.36	0.046174532
ESM1	2916	1.63	0.001608018	ADM	366	-1.36	0.00470981	AQP5	108	-1.26	0.002835895
NBEA	2705	1.19	8.67E-08	SPOCK3	361	1.13	1.60E-06	GRIN3A	107	1.82	7.24E-05
SEMA3B	2648	1.11	0.034303955	EML6	360	1.98	2.60E-05	COL4A4	107	1.63	0.020709488
KIAA1324	2567	1.05	0.046002021	EFNB3	359	1.42	2.22E-09	MSR1	106	1.38	0.022265735
KLF10	2556	-1.00	0.000327298	CDKN1C	358	-1.06	0.00094217	YBX2	106	-1.14	0.005416335
MAPT	2446	1.26	1.30E-05	PDE1C	354	1.01	0.00384597	ISG20	106	-1.69	2.21E-11
SYT13	2432	1.61	0.001407124	UCN3	351	2.13	0.0006727	DCDC1	106	1.08	0.008223956
SLC38A4	2415	1.85	1.12E-07	PEX5L	350	1.96	1.23E-05	KCNC2	105	2.56	3.10E-07
P4HA1	2399	-1.05	8.55E-09	SLC16A3	348	-1.08	0.0303094	ACSBG1	104	1.11	9.49E-06
ABCG1	2393	1.84	1.32E-17	PYY	340	1.84	0.00384693	KIAA0408	104	1.06	6.99E-07
APLP1	2385	1.45	1.27E-08	RYR2	340	1.62	0.00058985	DPEP2	104	1.83	0.00227507
PLA2G1B	2335	-4.40	6.79E-07	DPP10	338	1.82	7.32E-05	CPNE4	104	1.45	4.23E-06
GPR155	2329	-1.95	2.10E-06	GPRC5A	338	-1.44	2.81E-08	PLB1	104	1.62	0.002195334
GNAO1	2265	1.32	0.000423906	SYT17	336	1.02	0.00595851	LOXL1	103	-1.63	0.02054069
POSTN	2253	-1.66	0.009506177	SEZ6	335	1.65	0.00010062	E2F2	103	1.31	0.014392839
SPOCK2	2224	1.29	9.14E-13	TFF2	335	-2.10	0.02777322	LRCH2	103	1.03	0.006241905
CP	2042	2.08	3.27E-06	GPR63	321	-1.27	2.37E-05	ZFYVE28	103	1.04	5.96E-08
RFX6	1935	1.73	4.33E-08	SCIN	317	1.20	0.03770471	PTGFR	103	1.51	0.00027236
PCSK1N	1918	1.19	0.002851175	ANXA13	317	-1.23	0.00074333	DHH	102	1.06	0.008525261
CELF3	1874	1.52	1.39E-07	PRKAR2B	315	1.08	1.20E-07	ARC	102	-1.04	0.009319151
ABAT	1850	1.24	0.003597621	RARRES1	309	1.27	2.52E-06	GPR119	102	2.19	0.000402586
ZFP36	1833	-1.00	1.84E-07	CISH	309	-1.00	1.24E-07	SPRED3	102	1.29	0.000668792
RAB26	1827	1.20	0.001415	GPER1	308	-1.20	8.78E-07	KNDC1	102	1.40	4.90E-07
CACNA1H	1779	1.13	8.74E-08	CFAP74	305	1.48	5.11E-08	NCF2	100	1.34	0.003092975
SYT4	1759	1.72	5.21E-05	SYBU	301	1.10	2.56E-06	KIAA0319	100	1.47	8.56E-08
SCD	1735	1.32	3.71E-13	PLXDC2	300	1.16	1.98E-05	FGL2	99	1.05	0.001082771
GCA	1653	-1.37	0.000255357	PTGER3	295	1.06	0.00121363	C2orf88	99	1.31	0.00465216
C6orf222	1622	-1.00	0.025139127	BSN	294	1.34	1.22E-05	RELN	99	1.55	0.004595525
ATF5	1568	1.11	2.92E-05	OVOL1	291	-1.00	8.73E-05	CHRM4	99	1.04	6.90E-10
L1CAM	1560	1.53	1.09E-05	NALCN	283	1.48	0.00096486	THBS3	98	-1.02	2.37E-06
SFRP5	1550	1.11	0.036672417	SDF2L1	283	1.32	0.00357853	LRFN1	98	1.01	0.000116986
PFKFB2	1544	1.12	0.000216265	FFAR3	282	1.62	0.00017969	DNAH2	97	1.24	2.69E-07
MLXIPL	1538	1.63	4.97E-06	ADGRB2	272	1.30	8.54E-06	GALP	97	1.58	0.027773217
BDKRB2	1535	1.35	0.013714852	CDK5R2	269	1.58	4.27E-05	NPY	96	-1.07	0.031762907
SEZ6L2	1533	1.95	1.23E-05	TMEM130	267	1.18	0.00509481	APOD	94	1.25	0.019879981
BNIP3	1523	-1.30	2.02E-07	ETV5	264	1.25	2.87E-06	GEN1	94	1.05	0.027478448
NEUROD1	1502	1.60	0.000260308	GRM4	264	1.08	0.02799577	LYPD8	94	2.57	0.003553897
EPB41L3	1451	1.01	1.08E-05	COL17A1	264	-1.11	5.64E-10	NYAP2	94	1.08	0.020719956
KNG1	1431	2.25	0.00595851	ARG2	263	1.14	0.00049588	MAP3K15	94	1.72	2.47E-05
SYP	1430	1.26	0.000300146	E2F7	260	1.14	0.00469376	SCARA5	94	3.35	7.97E-12
BAIAP3	1417	1.28	8.03E-06	LYPD6	259	1.26	4.25E-05	TMEM229B	93	1.21	4.05E-12
KIF5C	1355	1.31	1.05E-13	PSD3	258	1.05	7.10E-06	DISP2	93	1.35	0.000321622

INSM1	1350	1.47	0.000687074	ITGB2	258	1.41	6.63E-05	A1CF	93	1.10	8.85E-06
CNTN3	1349	1.49	8.35E-05	GAL	258	1.52	0.00047739	PRKG2	92	1.00	0.000494842
SORL1	1339	1.53	4.52E-05	LGI4	254	1.06	0.00034762	LRRN1	91	1.49	0.000850859
ANKH	1328	1.15	2.51E-05	S100A13	253	-1.08	4.24E-05	C4BPB	89	1.61	0.00181821
PLCXD3	1304	1.91	0.000711893	SHCBP1	250	1.13	0.0460372	KCNF1	89	2.09	2.23E-05
PI15	1295	-1.06	0.01411393	SEMA5A	245	1.49	0.00113713	IL1A	88	2.37	0.03327108
MAN1A1	1287	1.01	6.39E-12	EML5	245	1.27	1.76E-05	BEGAIN	88	1.89	0.001384792
MYO3A	1284	2.02	0.005118268	PRND	244	3.83	9.97E-05	GABBR2	88	1.25	0.004874993
LRP11	1284	1.01	0.002564816	CHRNB2	240	1.30	0.00029253	CPA2	86	-2.33	0.00474465
DNER	1278	1.33	0.000122857	MYT1	237	1.74	6.65E-07	C20orf96	86	1.47	0.000748991
RAB3B	1270	1.66	1.71E-05	HMGCLL1	236	1.44	0.00141793	RUNX3	86	1.17	0.031762907
RF01957	1256	1.01	0.001533864	SVIP	233	1.13	1.66E-10	LINGO1	84	1.21	7.92E-05
OLFM1	1250	1.22	0.000381295	AURKB	233	1.03	0.00790766	PRRX2	84	-1.41	0.012810302
PGAP1	1245	1.24	4.16E-12	SLC35G2	231	1.27	0.00410937	DPP6	84	1.91	2.03E-11
VWF	1219	1.45	0.001463951	GABRB3	230	1.78	3.68E-06	SLC2A5	84	-2.69	0.000128839
RF01956	1209	1.00	0.001848365	C1QC	226	1.59	0.00038811	FGF10	83	1.06	0.000596194
ANXA10	1189	1.28	0.005310652	DNAH9	226	1.04	0.01301852	SLC18A3	83	1.43	0.004925154
OPCML	1179	1.55	0.030064295	TRABD2B	223	-2.14	1.54E-08	FSTL5	82	1.50	4.04E-05
NNAT	1171	1.18	0.001737584	SERPIND1	223	1.80	0.00011392	GPR75	82	1.02	0.000147712
GJD2	1153	1.92	0.004104282	CILP	221	-2.38	0.03486529	SYN2	81	1.21	6.73E-05
OLFM4	1133	1.86	0.03490004	FOLR1	221	1.47	7.38E-05	ATP1B2	81	1.03	3.23E-05
SCN7A	1101	2.36	5.85E-07	FOLR1	221	1.47	7.38E-05	CYTL1	81	1.58	0.048012805
CELSR3	1070	1.19	1.79E-06	BPIFA1	219	3.08	3.37E-09	CLCA1	80	1.97	0.032855565
AKAP12	1057	1.09	1.16E-06	IL17D	217	-1.01	2.08E-12	GHSR	80	1.35	0.005496077
MPZ	1044	1.73	2.88E-06	IGFBP1	217	1.35	0.03740481	RASGRF2	80	1.14	0.001458024
LIMCH1	1024	1.16	4.95E-05	HEYL	216	-1.45	0.02668806	EXTL1	80	1.18	0.004476919
SYT7	1018	1.37	0.000337864	KCNQ2	215	1.33	7.76E-10	PTPRC	79	1.42	0.002875498
ARFGEF3	1001	1.15	4.38E-07	MED12L	214	1.34	1.47E-07	PPP1R1B	78	-1.14	0.001691595
PLXNB3	999	1.35	0.001021019	TMPRSS11F	213	2.28	0.00072068	BRINP1	78	1.92	1.23E-05
ITIH5	998	1.38	0.003693384	TARSL2	211	-1.11	4.41E-05	ARPP21	78	1.34	0.016148675
METTL21A	993	-1.21	3.38E-15	CACNB2	210	1.05	0.00771981	PCP4	78	2.04	0.007877112
ATP2A3	980	1.08	0.011637524	FAM162B	210	1.30	0.00022402	ADAM11	77	1.47	7.36E-05
GCH1	954	1.12	0.000443629	FOXD3	207	1.00	0.04261734	KCNIP1	76	1.84	0.000646638
ADCY1	951	1.99	2.79E-08	CENPA	206	1.30	0.03165148	DIRAS2	76	1.11	0.020841174
TENM3	947	1.05	0.006627354	KCNA4	204	2.03	0.00525411	SYT14	76	1.61	2.85E-05
VWA5B2	915	1.79	2.45E-06	GALNT13	204	1.56	0.00011779	RAB7B	75	1.87	0.024109416
CACNA1A	913	1.39	0.000239361	AMPH	200	1.39	0.00026338	CNN1	75	-1.37	0.037032843
SHISAL1	906	1.47	8.18E-07	DISP3	199	1.39	0.0007406	PCDH10	74	1.10	0.000685641
SYT5	896	1.02	0.038458912	SCEL	199	1.62	3.81E-05	DOK6	74	1.52	0.003070209
MMP13	894	1.95	0.004819238	TENM4	199	1.14	0.00249608	MYRIP	74	1.22	2.11E-06
SYT11	886	1.00	0.000203752	DOCK11	198	1.02	0.00040362	CLEC2B	73	-1.75	2.19E-05
SGSM1	886	1.15	1.29E-11	KCNJ5	198	1.30	0.00930945	PNCK	73	1.18	2.40E-08
SCN9A	877	1.29	1.81E-10	MAPK4	197	1.14	1.16E-10	C5AR1	73	1.25	0.011915123
RGS6	873	1.12	0.001428865	INSC	195	1.29	0.00599134	RD3	72	1.56	0.004467751
TFR2	870	1.65	1.45E-17	SNAI1	195	-1.14	0.01722915	DIO2	72	1.89	0.004517532
CHL1	869	1.26	0.000192933	DAAM2	194	1.33	1.16E-05	ADAMTS20	71	1.89	0.021111122
PDE3B	853	1.24	3.15E-07	RFX2	194	1.12	0.00075801	ST6GALNAC	71	1.60	1.09E-05
RIMBP2	841	1.49	4.05E-06	C11orf87	194	1.72	7.97E-06	KCNG3	70	2.02	0.002997038
CASR	826	1.68	0.000132164	PRLR	192	1.44	0.00926864	SSTR2	70	1.54	0.00499625

HLF	820	1.01	5.08E-05	ATP8A1	191	1.28	4.10E-09	MYT1L	70	1.73	3.34E-05
TGFB3	820	-1.28	6.21E-11	OGDHL	191	1.62	8.90E-06	ADAM22	70	1.07	0.043957662
KCNK16	806	1.62	0.019310502	CFAP100	191	1.21	1.20E-08	HSD11B2	70	-1.13	0.007961975
ARHGEF9	803	1.12	0.0136123	TMEM132B	190	1.62	0.00618494	MAP7D2	70	1.36	0.000190757
SOWAHA	802	1.16	0.002102483	ADCK1	190	1.05	7.60E-09	KCNJ6	69	1.28	0.001315363
VCAM1	790	-1.19	0.000105868	CPA5	190	-2.96	5.26E-05	PHF24	69	1.10	0.001609276
TMEM59L	787	1.66	3.31E-11	CPA5	190	-2.96	5.26E-05	IL6	69	2.23	0.037432922
SLC29A4	787	1.49	5.36E-13	DSCAML1	189	1.50	4.35E-09	BTBD17	69	2.35	0.000663225
RF00100	778	-1.79	2.39E-17	SCUBE3	189	1.45	0.01027572	ADAMTS14	68	1.26	0.002570643
SNAP25	777	1.40	0.000555727	NEGR1	189	1.21	0.00031946	STK33	68	1.08	0.001010253
GADD45B	767	-1.04	0.005452667	AREG	189	1.34	0.04841124	SLC9A2	68	1.12	0.00062684
GRIK1	744	1.99	4.70E-05	CENPT	187	1.09	0.04460668	GIPR	68	1.79	7.58E-05
KCTD12	743	1.13	0.009518927	ARHGAP25	186	1.00	0.00271269	C1QL1	68	1.27	0.025749738
UPP1	736	-1.58	9.54E-13	CELF4	184	1.33	9.61E-09	PRLHR	67	1.50	0.000951339
RET	732	1.16	1.16E-05	C1QA	183	1.64	0.00011511	HHIPL2	67	1.86	0.00465216
NOL4	729	1.45	0.000297892	CKAP2L	181	1.11	0.01677571	B3GALT1	67	1.33	3.35E-10
PIP5K1B	728	1.29	3.53E-10	TMEM163	180	1.40	2.17E-06	CASKIN1	67	1.07	3.66E-05
ISL1	708	1.42	0.000993613	FRMD5	180	1.18	9.96E-05	PIK3CG	66	1.03	0.011618415
SDK1	671	1.13	5.67E-21	SYNDIG1L	180	1.48	0.01447735	COL13A1	66	1.10	2.01E-05
CADM3	671	1.80	1.18E-07	GPR158	179	1.15	0.00988449	ATP8A2	65	1.05	0.002547703
ADAMTS17	668	1.12	1.19E-06	CALB1	178	1.58	0.03290682	LYVE1	65	1.82	0.009230087
FRMD3	660	1.09	9.95E-09	APOH	178	1.12	0.04333916	SHISA7	65	1.32	0.000261586
TCN1	646	1.76	0.004448106	SLCO4A1	178	1.09	0.0018741	PHF21B	64	1.03	0.000170858
CLSTN3	643	1.20	0.001678968	CORIN	176	-2.06	0.006229	MYO7B	64	1.61	0.010077131
SLC30A8	638	1.47	0.039553389	IQSEC3	175	1.09	0.0051513	ARHGAP30	62	1.11	0.007544152
TMOD2	632	1.04	6.77E-05	RIMS2	175	1.03	1.61E-06	SHAS2	62	-1.56	0.04023123
GALNT18	626	1.05	0.003405027	HAP1	174	1.28	8.50E-07	REC8	62	1.04	0.002988398
RENBP	622	1.09	0.000509206	MATN4	174	-1.67	0.0157833	OTOP3	61	1.00	0.025416614
LSAMP	622	1.97	3.24E-06	GABRG2	174	1.56	7.08E-22	MAMDC2	61	1.14	0.007613573
DPP4	620	1.65	3.82E-05	ELAVL4	173	1.04	7.10E-08	FCER1G	61	1.43	0.001981893
SYNGAP1	617	1.14	7.39E-07	ACVR1C	171	1.57	0.01030005	DNAH5	61	1.46	5.75E-07
CHIA	613	2.10	6.64E-21	SRCIN1	170	1.70	0.00021018	IRX1	61	1.65	0.000186426
GDF15	613	1.58	0.002474495	ARX	170	1.08	0.01241824	RF00045	60	-1.09	0.002227552
P2RY14	610	1.49	0.00291304	TROAP	169	1.29	0.01000706	CLVS2	60	1.36	0.008662699
TANC2	608	1.07	0.000132809	PLPPR4	168	1.48	0.00276806	B3GALT2	60	1.69	0.002055995
CDH19	608	1.26	0.003847341	DCX	168	1.16	0.0156908	SLC5A7	60	1.30	0.000330563
CHST9	603	2.15	3.20E-07	GC	167	2.35	7.30E-31	GBA3	59	2.57	1.33E-05
ROBO2	602	1.29	0.015094277	SULT1C4	165	1.41	0.01774942	FREM1	59	1.81	0.005447663
MXRA8	600	-1.14	0.001570737	LSP1	164	-1.35	0.01781204	IRX4	59	-1.56	0.000508287
FHOD3	596	1.48	1.15E-05	SLITRK6	162	1.55	0.02056965	SVOP	58	1.44	0.000396107
FHL3	593	-1.03	2.12E-10	GKN3	161	2.50	5.78E-06	PADI1	57	1.62	0.039240735
ITIH4	591	1.39	0.003832495	HYKK	161	-1.19	0.00061925	UNC5D	57	1.31	8.95E-05
ANXA9	587	1.08	4.38E-07	KIF19	161	1.00	0.00062028	CMAH	57	2.09	8.56E-05
PLCB4	586	1.24	1.36E-08	MAST1	160	1.04	1.73E-05	RAC2	57	1.04	0.040451238
TRPA1	581	2.92	2.19E-05	MALRD1	157	2.36	1.04E-06	UNC45B	57	-1.15	0.017708824
LACTB	580	-1.70	3.90E-10	RAB39B	157	1.12	6.99E-07	WSCD2	56	1.35	0.046976153
SPTBN4	579	1.14	0.000135299	ATP1A2	157	1.47	0.00816475	TMEM117	56	1.12	0.00517301
ACTA2	577	-1.31	0.042303101	CCDC68	156	1.60	1.68E-06	NCAM2	56	1.48	1.74E-05
PCLAF	577	1.35	0.031762907	CCDC170	156	1.17	6.44E-05	CD163	56	1.02	0.025744294

UNC5A	576	1.29	0.001407124	CACNA1E	156	1.59	1.72E-05	PNMA2	55	1.23	1.28E-05
S100A14	574	-1.23	0.000599697	NRXN1	152	2.11	1.39E-10	DPT	55	-1.87	5.11E-06
PENK	569	1.88	6.77E-05	MIOX	151	1.05	0.00017792	VAV1	54	1.26	0.009144209
EGLN3	564	-1.06	0.002469478	LRRN2	150	1.47	1.17E-05	GABRR2	54	1.44	0.037836379
STMN3	562	1.15	0.001446791	SNTG1	149	1.27	0.00710962	TMIE	54	1.06	0.035561896
UNC80	561	1.66	0.000300001	SOX5	148	1.32	1.05E-06	SIDT1	53	1.41	0.031080008
PTF1A	560	-1.43	0.032880137	SSTR3	147	2.55	1.86E-09	SYTL5	53	-1.03	0.022428479
				GRIK2	147	1.39	7.20E-09	NTM	53	1.78	5.41E-05
								RAB39A	53	1.24	0.001708472
								TGM1	51	-2.54	8.64E-23
								PRR16	50	1.33	0.001262419

ESM Table 5: DEGs in NICCs isolated from 4 days old animals upon culture with fetuin-A

Gene	Base Mean	log2FC	p adjusted	Gene	Base Mean	log2FC	p adjusted	Gene	Base Mean	log2FC	p adjusted
GCG	277078	-4.06	5.61E-33	NEURL3	546	4.20	5.42E-07	LSP1	164	-2.34	0.000119046
ATP1A1	113022	1.10	2.93E-06	CPLX1	546	1.03	2.36E-05	ESCO2	164	-1.56	4.83E-09
CHGA	83091	-2.16	6.05E-13	IRX2	540	-2.15	4.71E-10	MKRN2OS	163	1.23	2.79E-07
CEL	69792	-2.94	0.011524988	POLE	536	-2.48	7.56E-18	GKN3	161	-2.98	1.51E-07
INS	43067	-2.23	0.0006457	LOX	528	1.00	0.042149294	KIF19	161	-1.41	5.50E-07
SST	36849	-2.10	2.34E-11	MAPK8IP2	527	-1.17	0.000183946	STC2	160	1.02	0.000379493
SPARC	35778	-1.13	0.021750423	ADGRL4	523	-1.06	0.045937794	PPP4R4	159	1.25	3.39E-06
COL3A1	28990	-3.37	4.16E-08	CA4	523	-1.92	0.000294972	ELN	159	-3.48	0.003445876
CFTR	28453	1.11	0.00058138	SLC25A53	518	-3.20	4.86E-31	MYBL1	159	-1.48	1.92E-08
CFD	21617	1.70	3.54E-05	TMEM151B	517	1.17	1.25E-18	KCNK3	159	-1.43	0.009331262
COL1A1	21532	-3.19	5.09E-06	CCNB1	515	-3.41	3.09E-24	SEMA4A	159	-1.15	3.22E-06
FN1	21369	-2.34	0.000209679	GAD2	507	-4.25	1.24E-32	CCNB3	158	-3.62	4.40E-17
CHGB	20938	-3.13	1.01E-30	SLC25A33	504	1.21	1.52E-07	ALDH1L1	158	1.00	0.028380052
TXNIP	19178	-1.40	8.10E-14	CDC42EP2	500	1.45	2.83E-12	MALRD1	157	-2.55	1.74E-07
COL6A3	17813	-3.29	8.86E-08	CD248	500	-2.12	3.24E-05	DUSP2	157	1.46	4.44E-06
COL1A2	16193	-2.81	5.93E-06	UPF3A	497	-1.10	1.47E-05	ARHGAP24	157	-1.04	4.07E-05
PCSK1	14037	-3.86	5.31E-43	PAK3	496	-1.20	0.000107782	CPED1	156	-1.96	0.000128548
DIRAS3	13930	-2.92	7.89E-28	CENPE	496	-2.71	4.56E-20	CCDC68	156	-1.43	7.46E-07
TM4SF4	13446	-1.21	8.36E-08	DUOX2	490	2.02	0.008520779	CACNA1E	156	-1.76	2.52E-06
CPE	13424	-2.32	7.97E-13	GPR160	489	-1.19	0.000593858	GPX8	155	-1.43	0.001035014
GATM	11443	-2.02	0.012985456	RAB9B	489	-2.58	4.12E-22	CDKN3	155	-1.40	5.38E-08
PCSK2	11191	-3.02	9.43E-17	EPPK1	486	1.12	0.047735623	KIAA1755	154	-2.91	0.000793464
DMBT1	10629	-1.24	0.041060281	ST8SIA1	485	-1.34	9.55E-10	CEP128	154	-1.19	2.60E-07
PPY	10557	-2.06	0.016447863	MAP6D1	482	-1.70	0.000910279	AGTR1	153	-1.71	0.006708463
TFRC	10342	1.28	1.35E-09	PLCG2	479	-1.07	5.67E-05	NRXN1	152	-1.62	1.21E-05
ACLY	10239	-1.29	3.69E-12	TSPAN18	477	-1.65	0.00089487	TMEM145	151	-1.07	0.000681621
SCG2	9725	-2.69	1.25E-18	SULF1	476	-1.67	0.001079832	MIOX	151	1.14	0.000585655
PEG10	9427	-2.50	1.96E-16	CLSPN	472	-1.76	9.97E-20	UCP2	151	-1.02	0.04991111
FGFR2	9406	1.39	3.39E-07	TNFAIP3	467	1.14	0.000910206	GUCA2B	151	-1.29	0.047626243
PAPPA2	8577	-3.44	5.43E-12	CPM	467	-1.61	6.83E-06	LRRN2	150	-1.58	5.19E-05
SCGN	8275	-2.73	8.53E-15	LRRC32	465	-1.79	0.003878596	DAB2	150	-1.16	0.00063944
MMP2	8243	-1.58	1.91E-06	KIF22	464	-2.05	2.57E-24	SNTG1	149	-2.03	1.57E-06
SCG5	8234	-1.46	5.95E-08	NCALD	463	-1.94	6.35E-09	SLPI	148	-1.25	0.004494813
HIF1A	7796	1.06	1.84E-18	CHAF1A	461	-1.55	2.63E-25	KLB	147	-1.78	1.75E-06
HMGN2	7484	-1.59	7.57E-20	CTSZ	461	-1.61	2.95E-06	SSTR3	147	-1.39	0.000632727
NUPR1	7448	1.54	5.55E-05	PLCD3	460	1.01	7.98E-06	ADGRV1	147	-1.78	9.55E-10
COL5A2	7390	-1.19	0.002546245	NEDD4	460	1.35	4.57E-16	DDIAS	145	-1.01	0.000119225
BIRC3	7312	1.36	8.07E-07	KIFC1	459	-2.48	1.20E-16	TNFAIP6	145	-1.58	0.001587416
BIRC3	7312	1.36	8.07E-07	GPX3	458	-3.07	9.18E-26	SPEF2	145	-1.14	1.27E-05
STOM	6925	1.30	4.35E-15	ASB9	457	-3.20	5.09E-14	FOXS1	145	-1.56	0.00031232
CTGF	6912	1.16	2.67E-11	AFP	457	-3.10	9.59E-08	RMI2	145	-2.94	3.52E-19
ARHGAP21	6759	1.13	0.000128494	FBLN7	455	-1.86	2.65E-11	CTHRC1	142	-1.87	0.000398648
COL5A1	6164	-1.94	0.000125757	ARHGEF28	452	1.10	1.25E-10	C6	141	-1.76	0.002603374
RALGAPA2	6032	1.07	1.27E-12	RBP4	450	1.55	9.44E-06	DEPDC1	141	-3.10	2.05E-15
VGF	5959	-2.29	1.25E-18	PPM1E	450	-2.36	1.67E-12	CCNE2	139	-1.48	9.45E-07
PGA5	5909	1.61	4.62E-07	FSD1L	449	-1.17	4.91E-13	TDRKH	139	-1.07	0.00082854
PRSS2	5768	-5.88	5.93E-08	CD74	448	-1.00	0.024384886	CDCA3	139	-3.41	1.12E-19

SLC7A8	5724	-1.89	1.05E-09	PKNOX2	446	-1.43	4.01E-05	UBE2T	137	-1.72	9.23E-08
PDGFRB	5569	-1.57	0.001915103	ALS2CL	446	1.26	0.000641243	KIF18A	137	-2.01	1.73E-10
CGNL1	5451	1.01	6.01E-05	TSPAN12	444	-1.09	0.000181598	SCML2	137	-1.09	3.81E-06
IGFBP4	5415	-2.52	1.86E-06	CHCHD10	444	1.11	1.90E-07	HCN4	137	-1.05	0.01971828
CTSC	5377	1.26	1.54E-05	PRICKLE2	443	-1.58	0.000124448	FAM184A	137	-1.53	8.68E-05
PMEPA1	5323	-1.20	7.81E-06	PRELID2	443	1.05	1.71E-06	CAPS2	137	-1.35	4.92E-09
SLC7A2	5273	-2.14	4.57E-13	KIF23	442	-1.89	4.22E-13	CENPO	136	-1.74	6.90E-14
HEPACAM2	5190	-2.51	1.43E-19	ACTA1	442	1.02	0.03718862	SLC8A2	136	-1.49	5.67E-05
BGN	5080	-2.85	0.000108854	C1S	442	-1.29	0.004394978	UABP-2	136	1.31	0.037674938
HMGA1	5046	1.58	4.41E-16	KIF20A	438	-3.10	8.12E-14	CBLN4	136	-1.86	0.014135776
STMN1	4959	-1.08	1.83E-14	EMB	433	-1.98	1.12E-09	ST8SIA3	136	-1.73	1.74E-08
TPD52	4880	-1.31	1.55E-10	ADAMTS12	428	-1.59	0.048490154	CCDC198	134	-1.17	4.77E-08
IER3	4857	1.37	0.000533401	KIAA1147	425	1.19	8.35E-10	MASTL	134	-3.13	3.07E-18
COL5A3	4843	-1.28	0.039243306	CCL2	424	1.11	0.000458862	BRIP1	134	-1.50	2.24E-08
CYR61	4739	2.36	4.94E-11	CMKLR1	422	-3.08	6.01E-05	DUOX1	134	2.60	3.83E-18
ANKRD1	4729	1.88	3.08E-06	HMMR	421	-3.08	6.86E-34	XRCC2	134	-1.65	9.44E-11
CREB3L1	4704	1.19	8.22E-08	PPP1R1A	420	-1.42	0.002828301	HCN3	133	-1.07	1.01E-05
CXCL8	4516	2.67	0.000896086	PIM1	418	2.39	9.48E-15	CDC6	133	-1.72	8.40E-11
FSTL1	4364	-2.15	9.85E-06	RADX	413	-1.79	1.23E-22	FBXO5	133	-1.83	9.44E-11
COL12A1	4350	-1.03	0.001042588	LRRC75A	412	1.33	1.36E-15	MELK	133	-2.24	1.06E-14
GRIA3	4295	-1.99	3.13E-09	SCN3A	411	-1.69	9.78E-13	KIF18B	132	-2.78	2.41E-10
MEST	4075	-1.53	4.41E-05	IQGAP3	408	-2.62	8.17E-25	EDIL3	132	-2.57	0.000101996
TTR	4028	-2.60	1.11E-25	CACNA1C	406	-1.19	0.001577069	LTC4S	132	-2.51	0.010836902
CTRC	3990	-3.50	0.00201389	MORC4	405	1.13	1.12E-12	FAM83D	132	-1.85	5.75E-09
CPLX2	3963	-1.83	7.29E-10	BRCA1	405	-1.45	2.94E-15	ASTN2	131	-2.32	4.07E-11
TF	3886	-3.05	2.09E-10	FAH	405	-1.13	5.14E-08	DTL	131	-3.41	1.80E-19
TP53BP2	3869	1.01	0.000218176	CLMP	404	-2.20	3.56E-10	BEX5	130	-2.42	3.39E-12
PTPRN	3830	-2.03	3.00E-19	KNTC1	403	-2.73	1.97E-18	IGFBPL1	130	-2.64	1.49E-08
CNTN1	3702	-2.02	3.81E-11	GNG4	403	-1.11	1.31E-06	BMPR1B	130	-1.75	0.00141468
KIFC3	3692	1.50	2.80E-05	BRINP2	401	-1.64	0.000506262	KIF26B	128	-1.06	0.015364084
SCG3	3684	-1.57	5.88E-10	C4BPA	399	1.13	0.039269246	CAMK1D	128	-1.07	0.026956826
RAP1GAP2	3679	-1.09	0.011806052	C4BPA	399	1.13	0.039269246	SPDL1	128	-1.48	3.07E-07
LRRN3	3662	-3.06	1.47E-15	TK1	399	-2.14	1.44E-20	PCK1	128	2.69	0.000385529
CBX6	3646	-1.12	1.88E-06	DLK1	398	-3.78	0.003701328	TMEM200A	128	-1.78	0.000453324
SDCBP2	3625	1.92	7.78E-07	FANCD2	398	-1.59	4.96E-14	GAS1	127	-1.50	2.07E-05
RGS4	3614	-1.49	3.67E-07	KIAA1324L	394	-1.02	2.61E-07	GRIK4	126	-1.77	0.00088173
PRXL2A	3584	1.04	7.85E-15	PHF19	393	-1.48	1.58E-12	SLC16A9	126	-5.29	8.65E-16
ABCC8	3418	-2.82	1.23E-12	SLC4A10	393	-1.20	0.016042266	MTFR2	126	-2.53	1.83E-13
PTPRN2	3355	-2.16	1.16E-12	CERKL	392	-1.96	1.03E-07	CDCA2	125	-2.04	1.37E-11
ICAM1	3298	1.70	1.93E-07	ADCY3	392	-1.56	3.75E-07	CITED4	125	1.89	0.020971848
SLC4A7	3264	1.26	1.47E-06	GOLGA7B	391	-1.28	6.31E-07	NRG1	125	1.26	0.004399301
CRIM1	3245	1.06	3.04E-07	NELL2	391	-2.35	2.30E-22	ABHD15	125	-1.53	0.000378941
SUN2	3223	1.10	5.53E-26	ADRA2B	389	-2.96	0.000544705	RASL11A	125	-1.07	8.44E-06
SOD2	3204	1.53	1.05E-14	ACADL	388	-1.03	2.33E-06	LEPR	124	-1.81	0.002024929
COL16A1	3108	-1.60	3.55E-07	INA	387	-1.06	7.78E-12	ADORA2B	124	1.35	0.000245354
GPRC5B	3099	1.27	9.88E-05	PBK	387	-3.16	1.45E-26	SPC24	124	-1.90	4.70E-08
PDK4	3096	-1.07	3.23E-10	SLIT2	386	-1.64	5.84E-11	CCDC60	123	-2.40	1.26E-07
TUSC3	3066	-1.14	1.23E-06	PROM2	384	1.33	0.000669518	CCDC60	123	-2.40	1.26E-07
TMPRSS2	3058	1.02	0.023655629	SLC4A8	384	-1.29	3.32E-06	MAGEL2	122	-1.71	3.23E-05

NPTX2	3042	-1.47	8.74E-13	NFASC	382	-1.57	3.19E-06	ASPN	122	-3.99	3.52E-05
SPIDR	3029	1.42	3.56E-07	STRIP2	381	-1.14	1.02E-10	SGO1	121	-3.54	2.03E-16
WWC1	2955	1.13	4.93E-09	MCRIP2	381	1.38	3.17E-13	JAKMIP2	121	-1.58	1.03E-05
PAX6	2938	-2.07	1.37E-10	KIF2C	381	-2.20	1.74E-11	CCR1	120	-1.24	0.014471831
ESM1	2916	-1.41	0.030695777	NCAPG	380	-2.00	8.16E-10	MYO1F	120	-1.33	0.001987001
RETREG1	2836	1.30	1.73E-21	LRRK2	380	-1.21	9.02E-07	SLC24A2	120	-3.33	3.95E-07
PXDN	2827	-1.02	0.017188826	RAPGEF4	377	1.08	0.000768686	KIF24	120	-2.03	5.62E-12
ANTXR1	2810	-1.69	2.90E-06	CAMK2B	376	-1.42	2.34E-11	IL1A	119	3.09	0.000884519
EREG	2804	1.01	0.000271879	SLC16A12	376	-2.08	0.001312308	BMX	118	-1.21	0.008095169
FBN1	2770	-2.43	3.68E-06	ITGA4	376	-2.19	4.72E-06	CENPU	118	-1.65	2.17E-11
SFRP1	2741	-2.82	2.36E-05	MXD3	375	-1.28	1.07E-09	NAP1L5	118	-1.21	0.000581142
SLC43A2	2685	-1.96	3.37E-09	LHFPL4	374	-1.85	3.88E-15	SLC18A1	118	-2.10	0.000108134
ARRDC4	2665	-1.09	9.29E-09	CYGB	373	-2.89	1.75E-05	ACTG2	118	-2.77	0.049943976
LTA4H	2627	1.10	3.34E-09	PLCL2	373	-2.17	3.40E-09	CDCA7	117	-1.13	0.000158513
F3	2618	1.00	0.000923559	TNR	371	-1.46	3.20E-05	LMCD1	117	-1.43	0.001967506
KIAA1324	2567	-2.66	8.53E-10	CABP7	368	-1.24	0.001553627	IRF5	117	1.00	0.020027228
EPS8L2	2561	1.45	1.62E-11	ADM	366	1.19	0.022758064	PRODH2	116	-1.35	2.58E-06
KLF10	2556	-1.44	1.53E-14	SLC39A5	365	-1.48	0.013561549	CENPS	116	-1.44	6.04E-07
ATP8	2488	-3.71	0.041721548	SLC39A8	365	1.35	0.003675912	C1QB	116	-1.74	2.38E-06
CEBPD	2470	1.57	3.71E-05	RASSF5	363	-1.00	0.000587039	FRMPD4	116	-1.35	0.041297891
SLC22A17	2468	-1.28	0.000131654	SLC35F3	361	-1.41	0.000644756	FRRS1L	115	-1.02	0.03577703
MAPT	2446	-1.35	6.03E-28	EML6	360	-1.94	2.66E-08	TRPC5	115	-1.54	0.001067882
BMP1	2445	-1.42	2.63E-07	CDKN1C	358	1.41	3.24E-06	MTHFD2L	114	1.15	1.81E-05
SYT13	2432	-2.27	1.85E-10	BVES	357	-1.98	0.002320713	TRPM6	114	1.57	5.45E-06
SLC38A4	2415	-1.63	3.79E-06	TIMELESS	357	-1.58	1.75E-05	ASTN1	114	-1.16	0.002211106
APLP1	2385	-1.11	7.95E-06	KIF4A	356	-2.81	5.15E-17	BST2	113	1.01	0.011715998
ANPEP	2340	-1.82	0.000491422	PDE1C	354	-1.02	1.22E-05	FAM221A	113	1.29	0.000118372
ALDH1A1	2299	2.19	0.000831526	SLC5A1	351	1.08	0.001171821	SLC5A9	113	1.07	0.004090949
SLC5A6	2282	1.18	9.24E-10	UCN3	351	-3.36	1.14E-15	NMB	113	1.12	0.010755605
GNAO1	2265	-1.78	3.58E-10	ARHGDIB	351	-1.82	0.000431957	HAPLN3	113	1.09	5.30E-06
POSTN	2253	-2.98	0.000501645	PEX5L	350	-1.63	0.000275594	MR1	112	1.00	0.034911782
ENPP2	2237	-1.43	0.018091478	BUB1	349	-3.16	4.79E-23	ZNF467	111	1.91	1.24E-10
IGFBP7	2165	-2.43	1.15E-05	CDCA5	349	-2.78	9.95E-29	SERPINA11	111	2.11	1.09E-06
MGST1	2134	1.17	1.55E-05	HK2	349	1.63	0.001549819	CAPN6	110	-4.24	0.000408586
GAS6	2121	1.24	4.72E-22	TBX3	349	-1.18	4.09E-05	CYP7B1	109	-1.19	0.003179528
ADAMTS4	2111	-1.07	0.011569647	IL33	348	-1.51	0.017172364	RBP5	109	-2.24	0.00808011
SNTB1	2096	-1.10	4.78E-05	GLB1L	345	-1.06	3.24E-10	DHRS3	109	2.21	2.44E-08
NFKBIA	2054	1.33	8.82E-05	RASL11B	343	-1.00	0.000752615	NT5E	108	-1.86	0.00630736
RGS5	2021	-2.28	0.000292509	CHTF18	343	-1.35	2.74E-18	SRPX2	108	-1.62	0.001185819
LIPA	1979	-1.02	2.45E-08	SGO2	341	-1.59	9.54E-10	ST8SIA2	108	-2.06	1.15E-07
UGCG	1969	1.01	1.88E-08	S1PR3	341	-1.80	0.00091143	P2RY2	108	1.86	1.16E-09
PFKFB3	1965	1.24	8.90E-07	PYY	340	-2.76	0.012070253	HAPLN1	107	-2.00	0.011617796
TRH	1948	-3.71	1.28E-12	LAMC3	339	-3.98	0.000224571	E2F8	107	-3.42	1.83E-19
TMEM30B	1920	1.47	6.99E-09	DPP10	338	-2.70	5.07E-12	COL4A4	107	2.30	0.000271341
COL14A1	1880	-1.41	3.43E-06	ASPM	338	-2.86	4.09E-16	MSR1	106	-2.53	1.88E-09
COL14A1	1880	-1.41	3.43E-06	SYT17	336	-1.40	1.89E-05	GLDC	106	-1.15	0.007988053
CELF3	1874	-1.15	1.48E-05	EFEMP1	336	-2.37	0.000354273	SLC19A3	106	1.27	0.000774913
ARRDC3	1858	-1.16	2.54E-12	SEZ6	335	-2.43	6.70E-30	YBX2	106	1.70	6.36E-05
APOE	1858	-2.09	1.42E-06	CITED1	335	-4.12	2.09E-16	NLRC5	106	-1.17	0.020265999

ABAT	1850	1.54	0.044683861	ZWILCH	331	-1.07	2.94E-07	VSTM4	105	-1.19	0.000593027
UNC5CL	1835	1.21	8.79E-05	DLGAP5	329	-2.71	3.16E-17	SCN4B	105	-3.52	4.60E-10
MCM6	1830	-1.50	1.44E-21	CNTLN	326	-1.74	2.67E-11	ERCC6L	105	-3.20	2.16E-19
RAB26	1827	-1.51	1.07E-13	SLC16A14	326	-2.38	2.53E-19	CENPW	104	-1.74	9.20E-06
PDX1	1823	-1.14	4.16E-13	RUNX1T1	325	-1.93	4.51E-08	SYNPO2	104	-1.69	0.003234721
IGFBP2	1802	-1.50	0.000377459	SLC8A1	325	-1.42	2.65E-09	DPEP2	104	-3.31	1.24E-12
TOP2A	1796	-3.26	1.62E-19	RAB29	325	1.21	6.41E-08	CPNE4	104	-1.57	1.92E-07
GJA1	1793	-1.10	0.000269759	FANCI	324	-1.09	1.02E-10	PLB1	104	-2.35	3.76E-07
LUM	1771	-2.72	6.24E-10	BUB1B	323	-3.26	2.99E-19	LOXL1	103	-2.18	0.003071386
THBS2	1769	-2.54	0.008832528	FANCA	322	-1.27	3.18E-12	E2F2	103	-3.04	2.63E-13
SYT4	1759	-1.49	2.61E-05	PLXNA4	322	-1.58	0.008104332	LRCH2	103	-1.28	0.003548154
PARD6B	1749	1.45	7.63E-10	ISG12(A)	321	1.58	2.22E-06	GFPT2	103	-2.04	5.80E-06
GNG2	1747	-1.33	3.78E-05	PDGFRA	321	-1.84	3.63E-05	AGT	103	-1.23	0.007842711
ECM1	1742	-1.19	0.002828936	KLF15	321	2.00	3.90E-18	PTGFR	103	-1.04	0.033667591
SESTD1	1732	1.31	3.75E-11	NUF2	320	-2.41	8.07E-20	BCAS1	103	-1.19	0.003862313
TINAGL1	1710	1.90	9.46E-08	MAML3	320	-1.21	0.000187157	CCDC65	102	-1.24	0.001522949
PPARGC1A	1702	1.36	5.54E-08	CERCAM	319	-1.19	1.61E-05	GPR119	102	-3.97	1.30E-11
KCNMA1	1701	-1.52	0.00010979	ANXA13	317	1.41	0.026032333	LGALS2	102	1.49	0.01579432
ENG	1694	-1.83	2.34E-06	ESPL1	317	-2.91	3.86E-15	SPRED3	102	-1.24	0.000298286
LAMB3	1688	1.04	0.008204303	FAM111A	315	-1.43	0.007616836	ATP6V1B1	101	-2.08	5.78E-07
DDC	1668	-1.55	2.04E-08	SHISA2	314	-1.89	1.94E-09	NCF2	100	-1.05	0.000831526
DNAJC12	1646	-1.79	5.33E-13	CIT	313	-2.27	8.08E-20	KIAA0319	100	-1.40	9.23E-07
LMNB1	1615	-1.09	2.42E-24	LIPH	310	1.11	0.013574894	ZGRF1	100	-2.71	5.73E-11
RND1	1605	1.31	0.000165222	UBE2C	310	-3.52	2.35E-15	EYA2	99	1.28	4.35E-06
OLFM4	1591	2.86	0.008113899	ANKS4B	308	-1.14	7.07E-06	PDYN	99	1.75	0.000920992
NRP1	1562	-1.59	2.31E-06	ZNF367	307	-3.06	1.14E-20	ARL4D	98	-2.15	2.65E-06
SFRP5	1550	-1.42	0.035354704	SPTB	306	-1.25	2.41E-05	PACRG	98	-1.72	1.96E-06
RAB31	1543	-1.59	6.82E-07	P2RY1	304	-1.94	1.20E-05	INKA1	97	-1.23	0.021180288
CDH11	1538	-3.60	8.07E-06	KIF15	302	-2.94	8.85E-21	GALP	97	-2.47	2.33E-06
MLXIPL	1538	-1.31	0.000639862	PLXDC2	300	-1.31	3.05E-08	KLHL41	96	-1.79	0.000284983
SEZ6L2	1533	-1.96	8.27E-12	EGFLAM	298	-3.11	1.25E-06	SLC2A12	95	1.39	0.026250446
CXCL14	1527	-3.07	3.53E-06	SPOCK1	297	-1.52	0.044886681	EXO1	95	-2.52	9.34E-13
PLVAP	1502	-1.32	0.000852303	PGBD5	296	-1.34	1.02E-08	LRRC49	94	-1.76	1.79E-07
NEUROD1	1502	-2.43	8.81E-18	COLEC12	296	-2.71	4.01E-08	GEN1	94	-2.12	1.39E-08
CDK18	1482	1.86	1.98E-17	DOCK8	293	-1.17	2.97E-05	NYAP2	94	-1.37	0.010829883
TGFBI	1466	-2.23	1.39E-12	IL17RB	292	1.43	1.86E-07	SCARA5	94	-1.16	0.007210632
FZD7	1456	1.00	2.32E-05	COL8A1	291	-3.41	0.000661264	ZWINT	93	-1.85	6.94E-07
CXCL2	1454	2.72	0.000378006	S100A4	291	1.41	0.000986054	DISP2	93	-1.96	4.55E-09
CXCL2	1454	2.72	0.000378006	MCM10	290	-2.02	1.02E-13	CPXM1	93	-2.18	0.008453551
MRC2	1453	-2.98	2.86E-05	PLSCR4	286	-1.29	0.000124456	A1CF	93	-1.15	0.000161919
COQ9	1450	1.04	9.72E-17	CHST11	286	-1.47	0.000130126	FAP	93	-3.06	0.000174348
PHYH	1444	1.10	7.70E-11	PCSK5	285	-1.50	2.95E-06	C3orf14	93	-1.16	0.000473221
SMC2	1444	-1.52	3.14E-13	ITGA1	284	-1.04	0.001409272	NPL	93	-1.47	3.97E-05
KNG1	1431	3.03	2.42E-07	NALCN	283	-1.91	4.11E-07	CALML4	93	-1.27	0.000166839
NOV	1431	1.82	7.00E-05	FEN1	283	-1.18	4.52E-08	CEP55	92	-1.98	9.82E-08
TANC1	1431	1.19	1.01E-14	ISLR	282	-4.84	0.000343361	CDC23	92	-1.04	0.000509225
SYP	1430	-1.25	5.28E-08	FFAR3	282	-2.18	1.73E-09	ARNTL2	91	-1.12	0.000145379
ADAM12	1418	-3.02	2.92E-06	FNDC1	282	-1.63	0.001549857	LRRN1	91	-1.48	0.000330998
BAIAP3	1417	-1.13	7.36E-05	PEAR1	281	-1.14	0.016226938	NPTX1	90	-1.45	0.001371209

PLAU	1399	1.28	3.14E-05	TTK	279	-3.31	6.22E-31	C4BPB	89	-2.78	6.58E-12
MCM4	1394	-1.45	2.71E-20	DDIT3	278	1.10	1.17E-06	KCNF1	89	1.90	0.000178609
COL15A1	1367	-1.76	0.000133802	CSPG4	278	-2.18	0.000435493	TSHZ3	89	-1.48	0.000287904
CNTN3	1349	-1.36	0.000150991	ROR2	277	-1.64	0.000104022	GABBR2	88	-1.56	3.48E-05
LRP4	1342	1.76	2.09E-18	E2F1	277	-2.80	4.31E-22	SAMD15	87	-1.46	9.55E-06
TMEM184A	1341	1.02	3.95E-09	ARHGAP33	277	-1.03	1.43E-07	HHIP	87	-1.58	0.01709187
ALDH1A3	1335	-3.49	9.04E-05	CDT1	276	-1.92	5.68E-21	SVEP1	87	-2.05	0.002449729
ANKH	1328	-1.21	5.21E-07	PDE4A	276	1.14	6.14E-10	C20orf96	86	-1.67	3.16E-05
EMILIN1	1318	-1.59	6.03E-05	ACP5	275	-1.97	0.000723012	DES	86	-3.39	0.027197789
BCL10	1309	1.09	2.31E-07	CENPH	274	-1.14	3.00E-09	KCP	85	1.78	0.000324202
PLCXD3	1304	-2.03	2.44E-16	ADGRB2	272	-1.13	3.28E-07	COL8A2	84	-3.62	0.000843115
HMGB2	1297	-1.67	4.94E-20	WNT7B	272	1.28	2.24E-10	SLC35D3	84	-1.14	0.010941957
CCL20	1293	3.70	3.44E-05	NEK2	271	-3.57	1.16E-20	FAM167A	84	-1.47	0.000352977
OXCT1	1290	1.03	8.62E-18	CDK5R2	269	-1.46	3.64E-05	PRRX2	84	-2.26	0.001844756
MYO3A	1284	-3.58	1.31E-16	TMEM130	267	-1.93	1.01E-10	PIMREG	84	-3.06	3.44E-11
LRP11	1284	-1.64	1.53E-14	MAP3K8	264	1.21	0.001083266	C7	83	-5.13	0.000230572
LCN2	1283	1.28	0.004893369	GRM4	264	-2.82	1.87E-17	HJURP	82	-4.15	1.56E-12
HTRA3	1273	-2.89	4.00E-14	CYP3A39	264	1.94	0.005749354	HPSE	82	-2.10	3.65E-09
RAB3B	1270	-1.81	2.45E-09	CYP3A39	264	1.94	0.005749354	PTCH2	81	-1.03	0.028445393
ERO1B	1263	-1.86	3.09E-10	CYP3A39	264	1.94	0.005749354	SKAP1	81	-1.41	0.002332145
VASH2	1262	-1.03	0.030597398	CYP3A39	264	1.94	0.005749354	F2RL2	81	-1.42	0.0079175
CA2	1253	1.05	1.21E-07	ARG2	263	1.23	2.06E-08	TMEM154	81	-1.38	2.50E-07
LIF	1243	1.63	0.00752078	DDR2	263	-1.12	0.000812293	TICRR	80	-2.16	7.32E-10
BCL6B	1237	-1.23	0.042300724	C1QTNF1	263	-1.33	0.000291865	GHSR	80	-2.04	0.000156124
CPEB2	1230	1.03	9.37E-07	LDHD	263	1.61	3.42E-14	BLOC1S3	80	1.21	0.009256559
PTGS2	1228	2.75	0.015108474	E2F7	260	-2.14	4.44E-14	EXTL1	80	-2.20	4.69E-07
PTN	1211	-2.61	4.08E-12	VRK1	260	-1.57	3.01E-22	PSMC3IP	79	-2.74	2.88E-13
NFKBIZ	1208	1.31	0.00132326	JAK3	259	1.78	4.82E-08	EFCAB8	79	1.68	0.003877492
FZD4	1195	1.15	7.10E-12	GJA4	259	-1.63	0.003055724	SSPO	79	1.10	0.018609181
ANXA10	1189	-2.35	4.33E-07	OXTR	257	-1.33	0.004084086	EPS8L1	79	1.03	0.014722634
ADAMTS1	1183	1.72	2.11E-10	ANO1	257	-2.82	4.81E-06	PTPRC	79	-1.20	0.044220518
OPCML	1179	-3.65	1.96E-07	MMP19	256	-1.05	0.025242478	BRINP1	78	-2.29	8.26E-10
NNAT	1171	-1.91	2.78E-12	CHAF1B	256	-1.27	7.32E-13	NRK	78	-3.99	5.78E-08
PLCD1	1168	1.17	7.20E-06	NDC80	255	-3.75	8.34E-26	LEF1	78	-2.18	0.000241468
NFKB2	1156	1.03	1.47E-07	E2F5	255	1.18	6.00E-06	ARPP21	78	-1.19	0.013561549
GJD2	1153	-2.71	5.21E-09	ITGA11	255	-4.02	5.80E-05	FOXJ1	78	1.07	0.010847788
NPNT	1144	-1.06	1.10E-05	PRKAG3	254	-1.46	9.75E-13	PCP4	78	2.81	2.48E-07
SFRP2	1143	-3.52	0.000866311	ROR1	254	-2.02	1.08E-05	CHADL	77	-1.38	0.002304125
KITLG	1137	-1.06	0.00081594	BICD1	253	-1.43	2.64E-05	MTBP	77	-2.99	7.81E-13
CDH17	1134	-1.60	6.06E-08	SHCBP1	250	-3.30	1.56E-18	NPY1R	77	-1.55	0.003814953
CRISPLD2	1134	-1.95	1.20E-05	NOVA1	248	-1.35	2.56E-06	RF00334	76	1.72	0.000661831
ANGPTL2	1127	-1.16	0.015243523	SLC7A4	247	-1.19	5.41E-08	DIRAS2	76	-1.99	4.60E-06
MYC	1119	1.72	1.12E-13	CRYBA2	246	-1.93	1.02E-12	SYT14	76	-1.04	0.001842306
PSD	1114	-1.22	4.92E-06	ASF1B	246	-3.65	4.56E-31	TRIL	75	-3.19	1.75E-06
FBLN1	1109	-1.23	9.65E-06	GPX7	246	-1.38	0.002106542	TRPC6	75	-1.22	0.026493185
SLC5A3	1108	2.70	2.96E-21	SPC25	245	-1.34	1.06E-09	HAS1	75	1.00	0.014593301
MCM2	1102	-2.23	3.19E-30	EML5	245	-1.06	7.47E-06	PCDH10	74	-1.11	0.006997921
ITGB3	1094	1.79	2.05E-12	GGT5	243	-1.78	0.000333322	DOK6	74	-2.85	5.21E-09
ANGPT2	1079	2.23	2.86E-12	KLHL32	243	-1.50	3.78E-09	HEMGN	74	-1.03	0.001031853

FAM169A	1065	-1.03	3.42E-07	CHST2	242	-1.02	0.014023627	C5AR1	73	-1.95	0.00012365
FBN2	1060	-1.80	8.01E-13	NEFL	242	-1.17	0.01515294	ABCG2	73	-1.30	0.000712793
FLNC	1030	1.24	0.000681621	CDCA8	242	-3.38	7.04E-20	HECTD2	73	-1.09	0.013971132
RPH3AL	1025	-1.11	3.17E-06	VDR	242	-2.45	4.38E-12	RD3	72	-2.29	2.68E-06
LIMCH1	1024	-1.12	2.15E-05	CHRNB2	240	-1.53	0.0002776	SERTAD4	72	-1.33	0.019729238
SYT7	1018	-1.26	4.83E-05	CCNB2	239	-3.50	1.40E-23	NUP210L	72	1.33	0.001709342
BEX4	1012	-1.41	1.04E-16	MYT1	237	-1.13	0.00797908	XKR5	72	-2.35	8.60E-09
TENT5C	1004	-1.78	7.25E-19	HMGCLL1	236	-1.62	3.90E-06	TMEM45A	72	-1.55	0.00014007
CCDC88A	980	-1.27	8.93E-08	MAP6	236	-1.74	1.88E-08	ADAMTS20	71	1.84	0.000152797
ATP2A3	980	-1.56	0.000400579	SERPINA6	236	2.45	2.43E-05	TRAIP	71	-2.00	2.38E-07
ROS1	969	-1.07	0.01341087	DIAPH3	234	-2.70	6.68E-17	ST6GALNAC	71	-1.68	3.90E-06
ADAMTS15	965	-1.30	6.06E-06	GAS2	234	-1.40	0.000148256	UNC5C	71	-1.95	2.91E-05
MARC2	957	1.16	0.020737432	AURKB	233	-1.71	8.85E-05	CCR7	71	-2.64	2.21E-07
GCH1	954	-1.29	2.15E-09	TCF19	232	-3.28	4.56E-31	DUOXA1	71	1.44	0.0456332
ADCY1	951	-1.05	0.011738752	CARMIL2	232	-1.12	9.70E-07	KCNG3	70	-1.64	0.006665948
ELMO1	949	-1.34	0.000528456	PPP1R3B	232	-1.08	0.000710902	SSTR2	70	-1.90	1.58E-05
ZBTB4	938	1.08	1.96E-12	SLC35G2	231	-2.02	1.91E-09	MYT1L	70	-1.35	0.003962842
TNFRSF11A	918	-2.30	2.85E-21	MDGA1	230	-1.59	0.000141007	PARPBP	70	-1.90	4.83E-06
VWA5B2	915	-1.84	6.54E-09	GABRB3	230	-1.54	0.000319744	ATP2B3	70	1.53	8.56E-08
CACNA1A	913	-1.58	5.55E-06	RECQL4	227	-1.79	6.94E-07	NEIL3	70	-2.64	2.13E-09
SHISAL1	906	-1.00	0.000250327	BIRC5	227	-1.61	4.55E-12	ADAM22	70	-1.76	2.78E-06
SYT5	896	-2.29	4.02E-19	C1QC	226	-1.48	0.000986054	HSD11B2	70	-1.09	0.004663082
MMP13	894	2.29	0.044886681	ATAD5	226	-1.26	1.64E-08	MAP7D2	70	-1.27	0.002983395
PCOLCE	892	-1.05	0.000661264	POC1A	225	-1.99	1.10E-19	FANCL	70	-1.10	0.000237357
ELK3	885	-1.12	0.000281603	SALL4	223	1.35	1.69E-06	KCNJ6	69	-1.26	0.019233513
FLYWCH1	883	1.12	1.38E-08	SERPIND1	223	-1.87	1.73E-09	FIGNL2	69	1.29	0.00143872
CDC14A	878	1.13	3.62E-12	PASK	222	-1.45	2.34E-10	SLC25A47	69	1.17	0.001582883
RGS6	873	1.33	8.23E-08	CILP	221	-3.87	0.000112157	ARL9	69	-1.04	0.008339725
SLC2A8	865	1.14	6.20E-06	MST1R	221	1.23	2.03E-10	IL6	69	2.99	0.000167792
HAPLN4	858	1.10	0.000168313	FOLR1	221	-1.82	1.81E-08	HTR2A	69	-1.88	7.55E-05
PDE3B	853	-1.25	6.36E-09	FOLR1	221	-1.82	1.81E-08	JAZF1	69	-1.68	4.63E-05
CDS1	849	1.04	0.000626414	PTGIS	220	-3.32	6.49E-07	BTBD17	69	-3.48	6.92E-09
CENPF	847	-2.83	1.57E-14	UBASH3B	219	-1.56	9.56E-13	PLEKHG6	68	1.36	0.000358597
DCN	840	-2.03	2.43E-05	TCF7L1	218	1.02	2.31E-05	STK33	68	-1.21	0.010060257
TPX2	839	-2.52	1.62E-26	TRPS1	218	-1.07	0.001054665	SLC9A2	68	-1.52	0.000342645
CCDC3	837	-2.15	6.33E-09	IL10RA	218	-1.06	4.35E-07	CFAP61	68	-1.39	0.000225563
TMEM223	827	1.22	6.00E-14	SSTR1	217	-2.64	1.09E-07	GIPR	68	-2.23	3.76E-07
CASR	826	-2.77	1.44E-18	PLK1	217	-2.58	5.89E-14	PLEKHD1	68	1.24	0.011524988
DTX1	823	-1.66	2.42E-24	NDST3	217	-5.12	1.79E-13	CEP72	68	-2.01	2.89E-07
PTGER4	815	-1.37	0.000910279	SRPX	216	-1.26	0.004204588	TYROBP	68	-1.36	0.00367116
CCNB1IP1	812	1.04	4.00E-14	HEYL	216	-3.25	2.85E-08	OGN	67	-1.66	0.04328517
TPM2	812	-1.48	0.049452441	PLA2R1	215	-2.14	0.00011766	DGAT2	67	1.68	0.000507582
CIP2A	810	-1.24	3.23E-16	GINS4	214	-1.18	1.14E-07	PRLHR	67	-1.73	0.000206979
KCNK16	806	-4.45	3.43E-12	ETV7	214	1.03	2.36E-06	HHIPL2	67	-2.48	0.000415968
PAPSS2	805	-1.48	1.27E-05	TMPRSS11F	213	2.93	1.53E-07	RBP1	67	-2.84	1.93E-07
ARHGEF9	803	-1.38	5.67E-08	MFAP2	213	-3.14	4.19E-06	DIRAS1	67	-1.51	0.006195372
SOWAHA	802	-1.42	4.67E-05	CPAMD8	211	-1.57	0.012957248	GFRA3	66	-2.72	0.006047769
DCXR	798	1.06	3.00E-07	CACNB2	210	-1.14	0.000276344	LYVE1	65	-2.39	1.50E-05
PIM3	797	1.26	1.59E-16	FBLN5	210	-1.23	0.011903336	SHISA7	65	-1.35	0.00122161

TSPYL5	796	-1.03	3.84E-06	FAM162B	210	-1.24	0.012155717	NKD1	65	-2.11	0.003443352
FKBP10	780	-1.03	0.02211151	IFNLR1	208	1.69	9.80E-12	CCSER1	65	1.11	0.00044914
MAFB	780	-2.43	1.54E-12	CCNF	207	-1.84	1.19E-12	CENPL	64	-1.89	4.03E-05
SNAP25	777	-1.29	1.36E-07	KIF14	207	-3.15	1.53E-14	PTCHD1	64	1.13	0.023350976
SORD	776	1.25	0.003590416	CENPA	206	-3.90	5.67E-21	COL28A1	63	-2.11	1.90E-05
UHRF1	776	-2.00	5.83E-24	P4HA3	206	-1.57	0.001151391	YDJC	63	1.07	0.00260513
GTF2IRD1	769	1.11	2.33E-08	NOX4	204	-1.23	0.000700235	CD37	63	1.67	0.001538919
MDFIC	752	-1.43	1.20E-06	KCNA4	204	-3.67	1.32E-12	C17orf53	63	-1.38	0.000131654
RGS16	751	-1.88	6.45E-13	GALNT13	204	-2.33	1.33E-09	ZNF550	63	1.30	0.001118647
EDNRA	747	-1.82	0.009083873	BARD1	203	-1.49	4.04E-07	TRPM8	63	1.19	0.001833687
PHLDA2	744	1.23	3.48E-15	AMPH	200	-1.58	1.46E-05	KCTD7	63	1.27	5.52E-06
GRIK1	744	-2.78	4.34E-21	MMS22L	200	-2.03	2.65E-14	SHAS2	62	-2.88	1.10E-05
MCM3	739	-1.78	2.84E-13	SCEL	199	1.14	0.000313121	REC8	62	-1.85	1.20E-05
ADGRA2	737	-1.26	0.026279667	CENPN	199	-1.77	1.38E-12	FANCB	62	-1.15	0.000962556
ELP4	731	-1.52	1.03E-07	MGP	199	-3.88	4.40E-06	CYTIP	61	-1.59	0.036762107
ATAD2	731	-1.44	4.36E-18	MMP16	198	-1.21	0.000772682	FCER1G	61	-1.35	0.028296857
NOL4	729	-2.10	1.03E-08	KCNJ5	198	-1.46	0.005472548	TCP11	61	1.67	0.013217273
SLC2A2	721	-2.70	4.65E-08	SIX4	197	1.54	4.40E-06	DNAH5	61	-1.19	0.013862075
FAM20A	716	-1.77	5.17E-10	DUSP9	196	-1.28	2.44E-05	IRX1	61	-2.39	1.02E-08
RACGAP1	714	-1.62	5.11E-16	CDH4	195	-1.75	0.000124456	TMEFF2	60	-2.15	1.57E-05
ABCC9	713	-1.69	7.93E-05	ADCYAP1R1	195	-1.37	0.000471073	GRM7	60	-2.36	9.99E-05
MEGF11	712	-3.49	1.40E-07	SNAI1	195	-1.57	0.000544445	GBA3	59	-1.96	0.029530093
SELENOM	711	-1.16	6.31E-07	DAAM2	194	-1.17	0.0127953	TOX2	59	1.76	5.90E-05
OSBPL10	710	1.18	0.00131852	RFX2	194	-1.43	0.000186046	FREM1	59	-2.44	0.001108352
MRPS6	709	1.10	1.27E-16	PIR	193	1.12	6.04E-06	SVOP	58	-1.08	0.028145973
ISL1	708	-2.28	4.52E-08	PRLR	192	-2.43	4.19E-13	RNF150	58	-1.02	0.031607365
KLK1	703	-3.67	6.34E-06	OGDHL	191	-1.64	1.31E-08	MMACHC	58	1.00	0.001555345
ROBO1	700	-1.32	0.00280632	NAP1L3	191	-1.33	0.000436185	TNFRSF9	57	-1.81	0.025015319
SH3BGRL	697	-1.40	2.91E-08	PRKG1	191	-2.45	3.64E-08	SHH	57	1.52	0.041160577
CACNA2D2	689	-2.22	5.78E-07	PCDH9	191	-1.13	1.32E-05	SMOC2	57	-2.26	0.001792299
ECT2	687	-1.14	8.53E-11	G6PC2	190	-7.74	3.90E-06	RAC2	57	1.64	0.037643574
SLC6A7	677	1.21	0.004369084	SCUBE3	189	-1.27	0.011261971	AARD	57	-2.34	0.002221894
ANLN	665	-1.31	6.19E-06	NEGR1	189	-1.63	9.93E-07	ZNF792	57	1.08	0.015003239
BEX1	662	-1.46	1.98E-19	SERPINF1	189	-2.03	0.00636327	WSCD2	56	-1.62	0.031051172
CKAP2	660	-2.51	8.63E-16	AREG	189	1.50	0.009449633	RNF39	56	1.25	0.004663082
KIF11	646	-2.16	1.35E-16	CENPT	187	-3.14	2.54E-24	ADAMTS3	56	-1.46	0.02273582
CLSTN3	643	-1.56	2.60E-07	HEY1	187	-1.16	0.02695452	ATP2B2	56	-1.09	0.010958717
RBPJL	640	-2.50	0.023201555	PPP1R3G	186	1.04	0.0011791	TMEM117	56	-1.59	0.000764288
SLC30A8	638	-3.69	3.91E-14	ORC1	184	-2.96	5.99E-19	SLC8A3	56	-1.67	0.001930826
NCAPD3	636	-1.36	3.02E-18	IRAK3	183	1.99	2.01E-09	LRRC17	56	-2.21	0.000449321
MYL9	629	1.09	0.027492259	C1QA	183	-1.44	0.002378304	VEGFD	56	-2.76	3.36E-09
GALNT18	626	-1.03	0.000539967	ITGA8	182	-3.11	7.75E-06	LVRN	56	-1.52	0.027936402
RENBP	622	1.24	3.42E-14	CKAP2L	181	-2.51	8.52E-14	ATP8B3	56	2.01	0.00084419
LSAMP	622	-1.06	7.28E-08	ADRA2A	180	-1.64	0.001511852	BMP5	55	-1.74	0.043487739
DPP4	620	-1.81	8.25E-17	FOXM1	180	-2.73	1.45E-14	TIMP4	55	-1.37	0.001266445
WNT5A	619	-1.30	0.003751764	SYNDIG1L	180	-1.49	0.002144044	CIDEA	54	1.62	0.007109185
GDF15	613	2.06	1.71E-06	FAM198B	180	-1.98	0.000128794	TCF21	54	-1.68	0.006108876
P2RY14	610	-2.96	4.17E-17	GPR158	179	-1.78	8.59E-08	GABRR2	54	-1.57	0.017162077
RTL5	606	-1.23	1.30E-06	ADAM33	179	-1.25	0.009197168	ZNF385D	54	-1.65	0.0168998

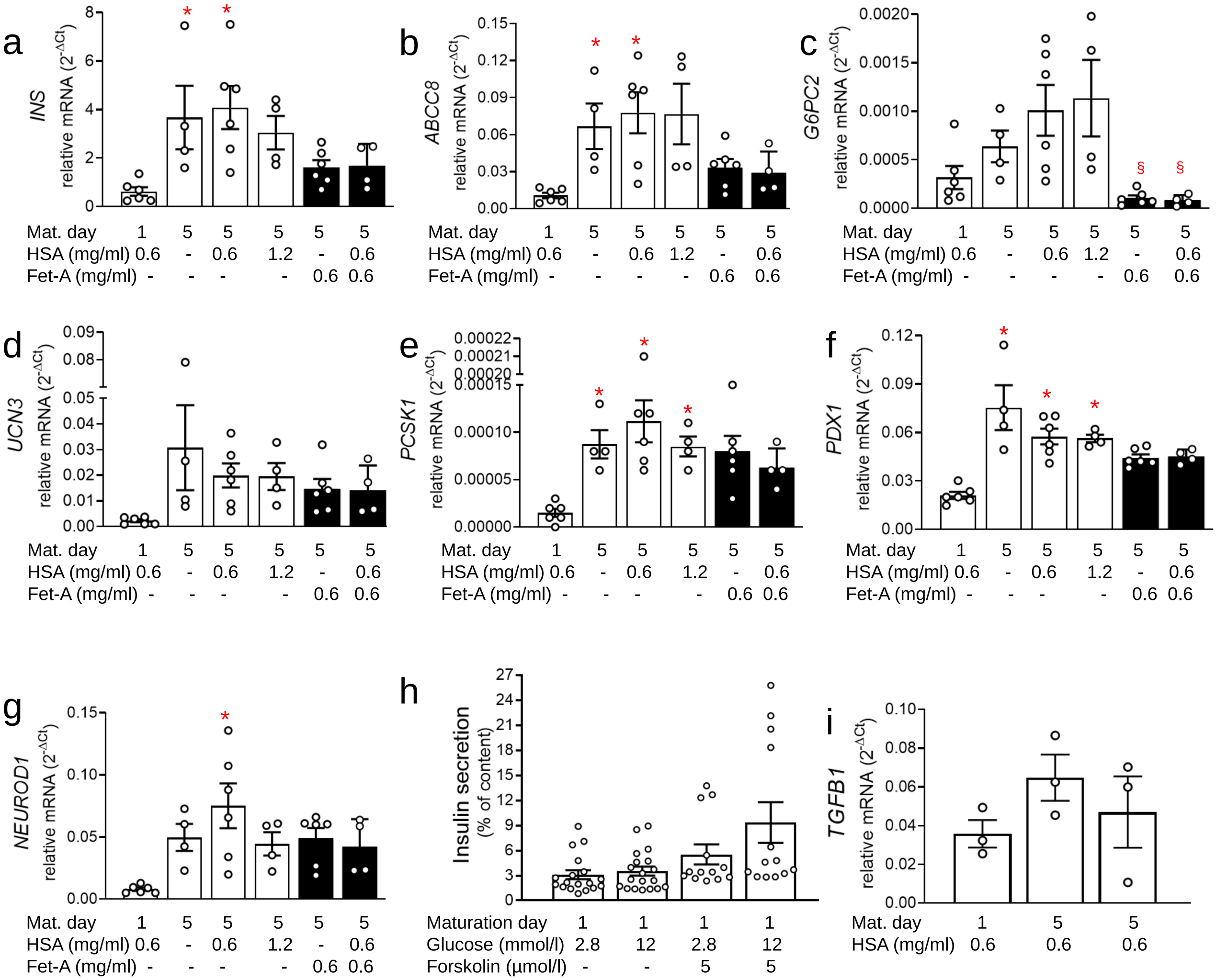
ITPRIPL1	603	1.21	9.86E-14	CALB1	178	-3.45	4.36E-08	TMIE	54	-2.66	7.26E-12
CHST9	603	-1.82	7.30E-09	ADGRA1	178	1.31	0.000259971	COCH	54	-2.09	0.047752248
ESRRA	602	1.17	3.51E-10	PTPRD	178	-1.67	0.005029138	SIDT1	53	-2.79	0.000151941
ROBO2	602	-3.10	4.61E-21	SLCO4A1	178	1.00	9.90E-05	DMRT3	53	-1.71	0.015227744
MBOAT1	601	1.11	5.37E-11	MARCH4	177	-3.22	5.12E-13	RAB39A	53	-1.84	3.79E-06
FHOD3	596	-1.28	1.17E-12	CORIN	176	-3.64	7.22E-08	SFTPB	53	-3.01	0.030733945
RUNDC3A	594	-1.10	1.46E-05	THBS4	175	-3.50	5.05E-05	SLC22A18	53	1.28	0.016967335
ITIH4	591	-1.61	0.000117109	IQSEC3	175	-1.57	8.60E-06	ABCA4	52	1.50	0.004987044
CDKN2C	587	-1.60	4.45E-11	POLQ	175	-2.65	7.70E-15	GPR83	52	-1.80	0.042837526
ZC3H12A	584	1.40	0.001231129	RAD51AP1	174	-1.71	1.57E-15	NKX2-3	51	-1.86	0.000385529
MAFF	581	2.23	3.12E-21	USP13	173	-1.07	0.013353808	GLI2	51	-2.87	1.56E-05
NCAPG2	579	-1.40	7.48E-14	ARHGEF39	172	-1.58	2.55E-08	PRR5L	50	-1.50	0.000902149
ACTA2	577	-2.38	0.036157429	LRRC10B	172	-1.09	0.002213132	CEP57L1	50	-1.55	0.000494108
PCLAF	577	-3.74	2.14E-50	WISP1	172	-2.22	0.002711061	STOX1	50	-1.13	0.001527958
UNC5A	576	-1.65	1.79E-07	PRR11	171	-2.75	2.13E-17	FAAP24	50	-1.53	0.001048094
COX7A1	576	1.06	1.06E-09	ACVR1C	171	-3.69	1.87E-17	MAFA	50	-1.87	0.031294365
S100A14	574	1.04	0.00042221	RAB40B	171	-1.25	2.06E-05	SLC11A1	50	-1.00	0.044471426
SGPP2	574	1.54	4.21E-05	AMBP	170	-1.34	0.009005139				
PENK	569	-2.70	7.78E-12	ARX	170	-1.64	0.002472531				
CXCL12	567	-1.09	6.86E-06	SERPINB9	169	-1.02	0.022511712				
STMN3	562	-1.40	3.71E-05	TROAP	169	-2.87	5.65E-16				
UNC80	561	-2.31	3.52E-10	PLPPR4	168	-2.64	2.85E-09				
SGCB	560	-1.03	0.001514725	DCX	168	-1.58	0.00551381				
LARGE2	558	1.06	7.70E-06	EVA1C	167	1.76	6.19E-06				
PXDC1	557	1.03	0.009461968	GADD45G	166	-1.67	1.77E-07				
SLC7A14	556	-2.76	3.63E-19	SULT1C4	165	-3.24	1.31E-10				
KIF20B	552	-1.04	1.53E-10								
KCNH6	551	-2.01	1.24E-09								
EID1	549	-1.02	0.006999657								

ESM Table 6: DEGs in NICCs isolated from 4 days old animals following culture with SB431542

Gene	base Mean	log2FC	p adjusted	Gene	base Mean	log2FC	p adjusted	Gene	base Mean	log2FC	p adjusted
MMP7	39682	-1.36	0.035276836	LOX	528	-1.63	0.002228017	GUCA2B	151	3.36	1.12E-09
CFD	21617	1.27	0.009731162	LDLR	491	1.29	0.002268006	KCNA6	150	-2.11	0.002618947
FN1	21369	-2.57	0.000198704	RAB9B	489	-1.03	0.000744777	IRF8	150	1.35	0.026840531
ANXA4	15152	1.03	2.33E-05	SULF1	476	-1.87	0.000963627	DAB2	150	-1.26	0.000883438
DIRAS3	13930	-1.17	0.000199168	ESPN	468	1.64	0.000763767	FMOD	149	-1.32	0.008065442
OLFML2A	8352	-1.32	0.000993603	LRRC32	465	-1.79	0.013486796	SOX5	148	-1.00	0.005558204
NUPR1	7448	1.26	0.004782783	PNLIPRP1	458	1.61	2.61E-11	SLPI	148	-1.84	0.000102646
COL5A2	7390	-1.21	0.007800906	CTSL	457	-1.14	0.000300205	TNFAIP6	145	-2.82	7.78E-08
PKHD1	6963	-1.61	3.91E-14	AFP	457	2.47	3.73E-05	FOXS1	145	-1.48	0.002618947
IL1R1	6724	-1.17	1.24E-05	FBLN7	455	1.32	7.14E-06	NEURL1B	144	1.62	0.000364071
THBS1	6466	-2.17	6.08E-29	C1orf115	455	1.42	5.62E-08	GYPC	143	1.42	5.86E-07
SPHK1	6415	1.38	3.99E-20	EPHA4	450	-1.17	1.34E-05	CTHRC1	142	-1.45	0.021844979
COL5A1	6164	-1.44	0.019515584	ACTA1	442	-1.91	0.000214448	MT3	139	2.31	0.023155338
SLC7A8	5724	-1.29	0.000272898	C1S	442	1.50	0.00210357	C11orf96	138	1.06	0.036567994
PMEPA1	5323	-3.16	2.09E-35	RNASE4	427	1.31	0.007561183	GPR39	138	-1.12	0.000514602
CYR61	4739	-1.00	0.033922162	CCL2	424	-1.43	4.94E-05	EFS	137	-1.13	0.016246885
TNC	4663	-3.15	9.72E-08	CLMP	404	-2.37	7.37E-11	UABP-2	136	-1.97	0.005431187
FSTL1	4364	-1.53	0.008837579	TGFB2	391	-1.01	0.000398511	CBLN4	136	-3.47	1.07E-05
COL12A1	4350	-2.19	5.21E-13	CYGB	373	2.67	0.000105408	SAMD11	136	-1.31	0.008507162
PTK7	4202	-1.09	1.76E-06	UCN3	351	-1.04	0.047176314	EBF1	132	2.13	1.58E-05
BMF	3665	-1.65	5.99E-14	HSF4	350	1.53	0.023458296	EDIL3	132	-3.37	1.86E-06
RGS4	3614	-1.08	0.001492554	RYR2	340	-1.14	0.012380366	BMPR1B	130	-2.99	3.48E-07
ABCC8	3418	-1.08	0.038379868	FAM124A	326	-1.11	6.14E-05	VGLL1	129	-1.08	0.000416422
LTBP1	3406	-1.50	0.000754091	PLXNA4	322	-2.12	0.001050457	TRPC4	127	-1.32	7.16E-08
NEDD9	3248	-1.15	0.000458717	EDN1	322	-1.80	5.69E-09	SLC16A9	126	-2.09	0.000120851
COL16A1	3108	-2.29	5.76E-13	PDGFRA	321	-1.28	0.018840092	GDNF	124	-1.84	0.00029544
C14orf132	3099	-1.08	4.89E-09	KLF15	321	1.11	3.99E-05	LIPG	122	-2.29	4.91E-06
ANTXR1	2810	-1.20	0.004919819	ADCY7	315	-1.67	7.19E-15	NFATC1	122	-1.11	0.012853208
SFRP1	2741	-2.26	0.003729171	ITGA7	304	1.68	0.003262811	ASPN	122	-3.49	0.001245145
SLC1A1	2520	-1.09	0.01272644	P2RY1	304	-1.21	0.027259573	PPP1R14A	118	1.14	0.024197387
LOXL2	2339	-1.42	8.60E-05	ACSL5	302	1.03	0.008000803	TM7SF2	117	-1.34	1.00E-05
PLA2G1B	2335	2.41	8.77E-05	TNFAIP8L1	302	1.11	0.02107044	LMCD1	117	-1.14	0.046799531
ENPP2	2237	-1.54	0.032247923	BMP4	298	-1.12	2.82E-07	S100A12	115	-6.09	1.01E-10
PHGDH	2047	1.13	2.27E-24	CAVIN3	296	1.37	0.009636192	CES3	114	1.49	0.000654592
CP	2042	-1.67	0.001089954	NPC1L1	292	1.29	0.014376763	RUNX2	110	-1.45	0.048947126
TRH	1948	-7.44	1.11E-45	COL8A1	291	-5.90	1.78E-08	RBP5	109	2.27	0.008837579
ENTPD5	1818	1.33	0.000327368	CLMN	288	-1.64	7.45E-08	NT5E	108	-2.81	0.000117717
LUM	1771	-2.33	1.19E-06	CHST11	286	-1.55	0.000247378	SRPX2	108	-3.03	1.26E-08
THBS2	1769	-4.40	9.80E-06	MASP2	285	1.22	0.036871886	ALOX15	107	-1.26	0.011367558
ECM1	1742	-1.77	2.62E-05	ITGA1	284	-1.85	2.25E-08	ALOX15	107	-1.26	0.011367558
IL11	1727	-2.62	5.21E-13	FNDC1	282	-1.78	0.002157441	GCNT1	106	-1.70	0.014295166
TINAGL1	1710	1.50	0.000193293	PEAR1	281	1.97	1.99E-05	PLA1A	106	1.10	0.000771802
ENG	1694	-1.73	5.28E-05	DDIT3	278	1.02	5.25E-05	SCN4B	105	-4.61	5.16E-14
PLAUR	1677	-1.10	2.99E-07	PLA2G4A	271	-1.28	0.003262811	KCNV1	105	-1.74	0.000172688
NTN4	1620	-1.19	6.13E-13	ADAMTS6	261	-1.64	1.30E-10	CARD11	104	-1.58	0.002106542
VCAN	1585	-1.39	9.85E-05	RHPN1	258	-1.30	0.00165217	PLB1	104	-1.22	0.027109274
VCAN	1585	-1.39	9.85E-05	OXTR	257	-1.26	0.021836615	LOXL1	103	-2.39	0.00468944

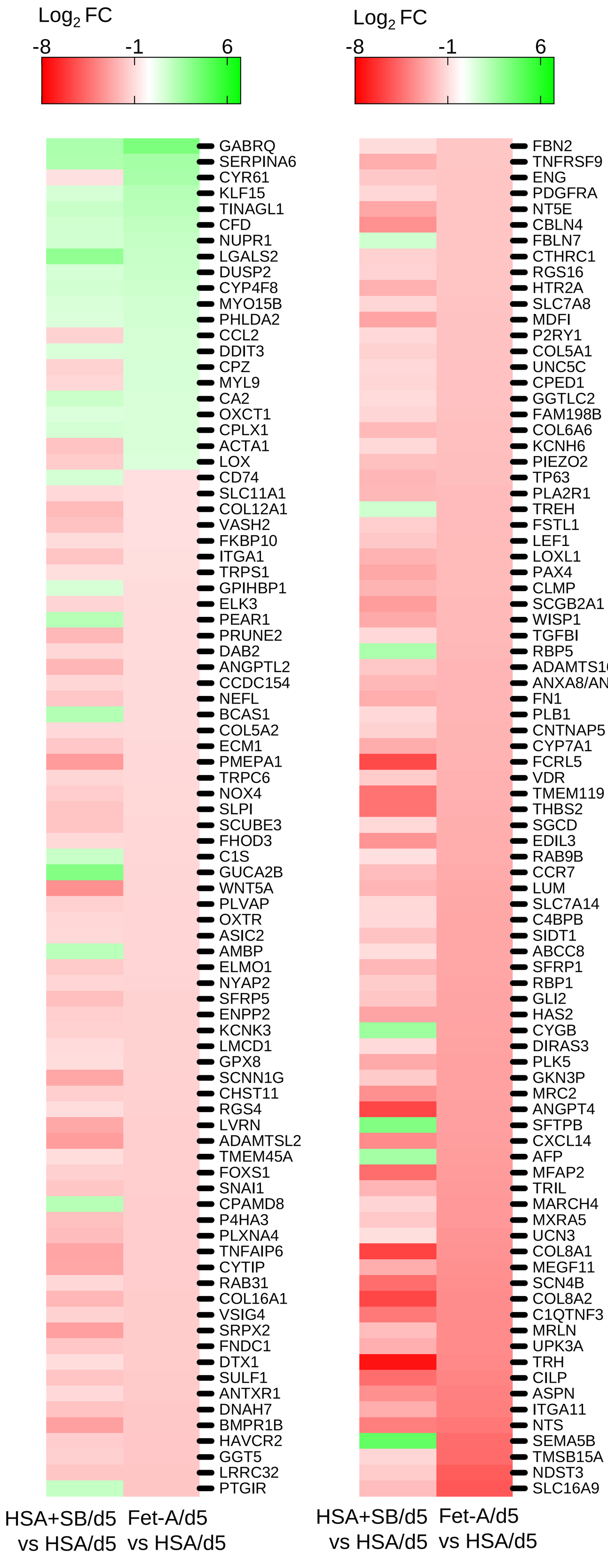
ATF5	1568	1.19	2.22E-07	ITGA11	255	-2.59	0.037339258	BCAS1	103	2.09	5.33E-10
SFRP5	1550	-2.02	0.006593964	PRND	244	2.68	0.019002953	NEXN	102	-2.95	6.19E-11
LPL	1544	1.61	4.11E-05	GGT5	243	-1.49	0.011669961	ARC	102	1.16	0.000511845
RAB31	1543	-1.26	0.000568688	NEFL	242	-1.76	0.000653904	LGALS2	102	3.00	6.71E-07
BDKRB2	1535	-1.95	1.83E-21	VDR	242	-1.64	2.80E-05	COL11A1	100	-1.95	0.008773164
CXCL14	1527	-3.65	1.54E-07	SMAD7	240	-2.86	1.90E-17	MMP28	97	-1.84	0.005830279
PLVAP	1502	-1.50	0.000572775	SERPINA6	236	2.21	0.000745241	ITPKA	96	1.42	0.01637757
TGFBI	1466	-1.22	0.000953076	LDB2	234	1.42	0.028915185	LYPD8	94	2.51	5.57E-06
MRC2	1453	-3.50	4.57E-06	OLFML2B	228	-2.40	0.000492723	NYAP2	94	-1.33	0.039101955
TACSTD2	1444	1.14	3.58E-10	SLA-DQB1	225	1.33	0.043184419	IL2RA	91	-1.34	0.008435952
FSTL3	1342	-1.38	1.70E-12	APOLD1	222	1.56	0.000754091	C4BPB	89	-1.20	0.006699821
SKIL	1331	-2.30	8.14E-35	CILP	221	-4.60	3.20E-05	MSC	89	-2.37	4.50E-12
OXCT1	1290	1.01	4.55E-16	DEPP1	221	1.54	0.003950258	BEGAIN	88	-1.31	0.02576501
VASH2	1262	-1.94	6.26E-05	GUCA2A	221	4.20	3.41E-05	COL8A2	84	-5.81	3.21E-06
CA2	1253	1.44	5.03E-13	LTBP2	219	-1.55	0.00363448	CAMK1G	84	-1.27	0.008773164
VWF	1219	1.08	0.034320026	TRPS1	218	-1.04	0.005461917	S1PR5	82	1.60	0.000312144
LAMA3	1189	-1.21	2.81E-20	BDKRB1	218	-2.81	9.20E-15	BCL2L15	81	1.13	0.000664274
SERPINE2	1183	-1.65	3.06E-05	NDST3	217	-1.64	0.03504068	STAC	80	-2.98	2.87E-06
GSTA2	1129	2.33	4.91E-07	PLA2R1	215	-2.23	0.000269902	BLOC1S3	80	1.20	0.03041282
GSTA2	1129	2.33	4.91E-07	MFAP2	213	-4.59	1.50E-10	NHS	79	-1.80	0.010813307
GSTA2	1129	2.33	4.91E-07	HGF	211	-1.42	0.000793024	LEF1	78	-1.76	0.011781151
ANGPTL2	1127	-2.31	1.45E-06	CPAMD8	211	1.97	0.003234632	BNC2	77	-1.78	0.037591422
PALLD	1122	-1.10	0.008742252	NAV3	211	-1.28	0.034522343	TRIL	75	-2.34	0.001710407
FBN2	1060	-1.10	0.00012795	FILIP1	210	1.38	0.020236534	RAB7B	75	2.44	1.26E-08
PPP1R16B	1042	1.26	0.008354745	EPHB6	210	-1.30	5.17E-05	TRPC6	75	-1.31	0.047264181
DCLK1	949	-1.18	0.039101955	ARSI	210	-1.69	0.035276836	CLEC2B	73	1.47	0.002027844
ELMO1	949	-1.69	5.16E-05	P4HA3	206	-2.01	0.000123844	CRYBG2	73	1.81	6.30E-05
	890	-1.35	2.87E-05	NOX4	204	-1.60	4.63E-05	DIO2	72	-3.38	4.11E-14
ELK3	885	-1.36	4.84E-05	DISP3	199	-1.25	0.027117052	TMEM45A	72	-1.08	0.024542782
MEGF6	874	-1.01	6.57E-05	COX6B2	197	-1.47	6.19E-11	ACE2	71	1.77	5.33E-06
CEMIP	834	-2.45	5.41E-07	SNAI1	195	-1.79	0.000313776	UNC5C	71	-1.21	0.031814089
DTX1	823	-1.10	1.51E-10	PTP4A3	191	1.25	0.016755396	CCR7	71	-2.09	0.00017681
GRIP1	785	-1.00	1.08E-15	SCUBE3	189	-1.83	0.000754091	SSUH2	71	1.84	0.01637757
FKBP10	780	-1.10	0.040370049	FAM198B	180	-1.29	0.044817348	IL34	70	1.49	0.004179728
INHBA	773	-3.70	1.51E-45	ZNF469	177	-1.02	0.002031613	PHF24	69	-1.05	0.013128072
GADD45B	767	-1.36	0.005021651	MARCH4	177	-1.37	0.00762695	SMPD2	69	1.14	0.038718259
RGS16	751	-1.40	9.63E-07	MYCL	176	-1.11	0.012299152	HTR2A	69	-2.47	2.31E-06
PHLDA2	744	1.01	1.61E-09	HLA-DRA	176	2.06	0.015918259	EHD3	68	-1.01	0.018308176
SPSB1	740	-1.41	3.92E-09	FZD2	173	-1.13	0.000123462	RBP1	67	-1.61	0.012038034
MEGF11	712	-2.57	0.000678893	PTGS1	173	-2.43	2.13E-05	S100A9	66	-3.90	9.85E-05
GRB7	667	-1.00	3.96E-05	WISP1	172	-2.68	0.001017358	SHAS2	62	-2.88	6.26E-05
EGF	637	1.40	0.009690906	IRAK2	172	1.23	0.002018411	OTOP3	61	1.11	0.049390041
MYL9	629	-1.27	0.028088014	AMBP	170	1.88	0.000291598	CYTIP	61	-2.81	0.000557332
WNT5A	619	-3.49	5.20E-16	KANK3	168	1.11	0.011941447	NAAA	58	-1.39	0.000175945
CHST1	615	1.48	0.000283294	FOXF1	166	-1.12	0.000586638	PADI1	57	-2.41	0.007147303
C1R	597	1.65	5.58E-07	LSP1	164	-1.54	0.040377346	TNFRSF9	57	-2.60	0.003948809
FHOD3	596	-1.25	2.40E-11	SRGN	163	-1.80	0.00058275	TLR2	57	-1.90	0.000116677
HABP2	594	-1.49	2.08E-12	SLITRK6	162	-2.35	0.001103736	NRROS	56	1.46	0.0149231
AEBP1	578	-2.35	0.00016883	GKN3	161	-1.67	0.015146958	ALPL	56	-2.37	0.007322529

SERPINE1	576	-1.91	9.58E-05	LYPD1	160	-1.01	9.27E-05	LVRN	56	-2.73	0.000295003
FABP5	569	1.36	0.013211519	SNED1	160	1.43	1.05E-06	CUX2	54	-1.94	0.009367197
SLC7A14	556	-1.24	0.000491299	RASL12	160	1.66	0.008773164	CNTFR	54	1.38	0.019720629
KCNH6	551	-1.24	0.001317038	KCNK3	159	-1.46	0.024248803	SIDT1	53	-1.91	0.026601761
CPLX1	546	1.17	7.98E-06	DUSP2	157	1.14	0.002223723	NHSL2	53	1.28	0.002230638
INHBB	535	1.32	0.001050457	CPED1	156	-1.31	0.038532699	SFTPB	53	3.42	8.43E-08
CYS1	531	-1.17	2.89E-16	GPX8	155	-1.07	0.047493418	GLI2	51	-1.80	0.02044867
				C21orf62	153	-1.27	0.03291443	ABI3BP	50	2.58	4.43E-05
								SLC11A1	50	-1.19	0.044368604



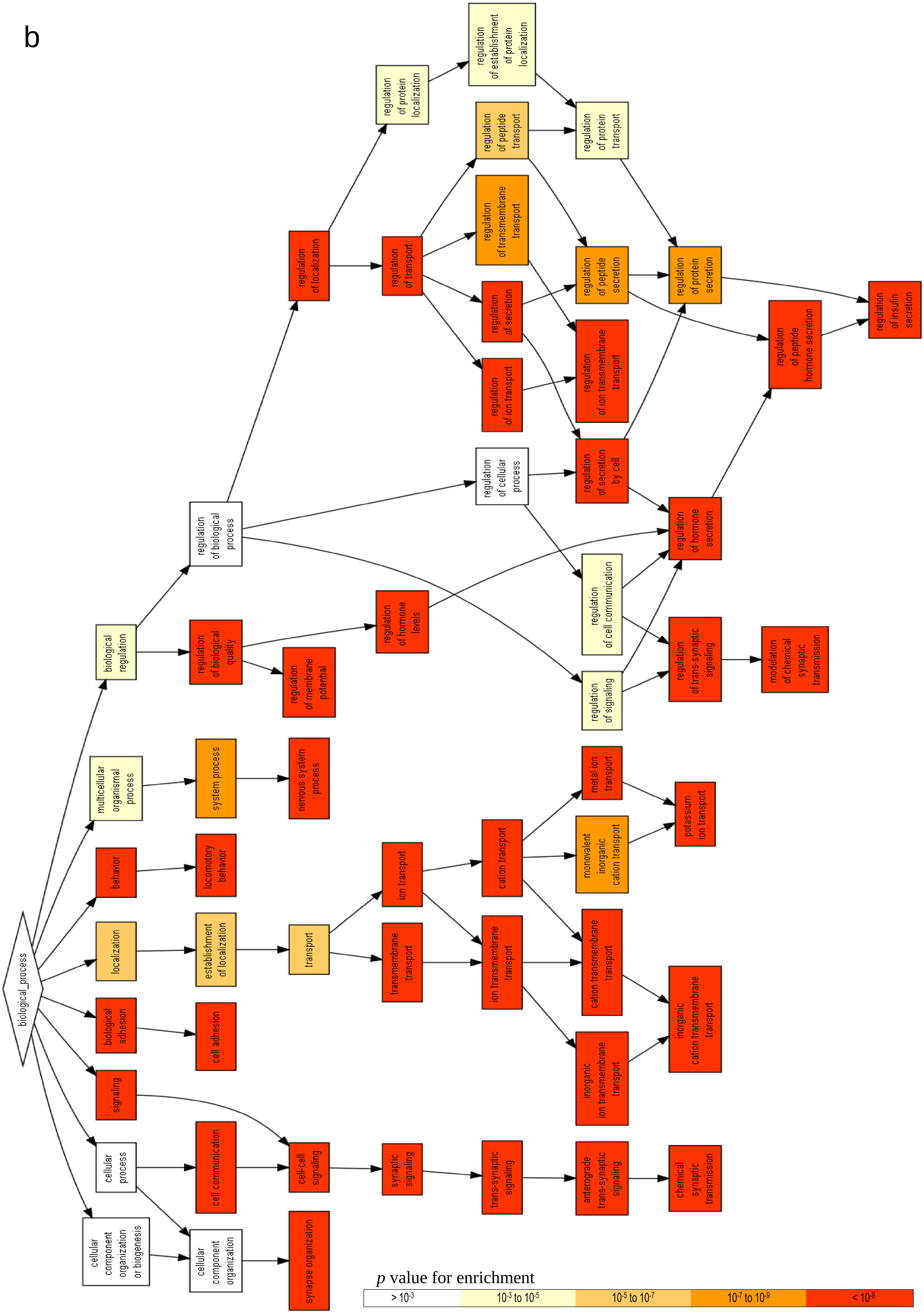
ESM Figure 1 Functional maturation of NICCs does not depend on HSA. (a-g, i) NICCs were maturated for 5d in HSA-free medium or in medium supplemented with human serum albumin (HSA) or fetuin-A (Fet-A) at different concentrations as indicated and described under Methods. (a-g, i) Relative mRNA levels (ΔCt against RPS13) assessed by RT-PCR of (a) *INS* (insulin), (b) *ABCC8*, (c) *G6PC2*, (d) *UCN3*, (e) *PCSK1*, (f) *PDX1*, (g) *NEUROD1* and (i) *TGFB1* and expressed as mean ± SEM of (a-g) n = 6 and (i) n = 3 independent NICCs preparations (h) Insulin secretion expressed as % of insulin content of immature NICCs (HSA/d1) cultured in standard medium and presented as mean ± SEM of n = 13-19 replicates out of 6 independent NICCs preparations. $p < 0.05$ * significant vs maturation d1; § vs respective maturation d5.

a



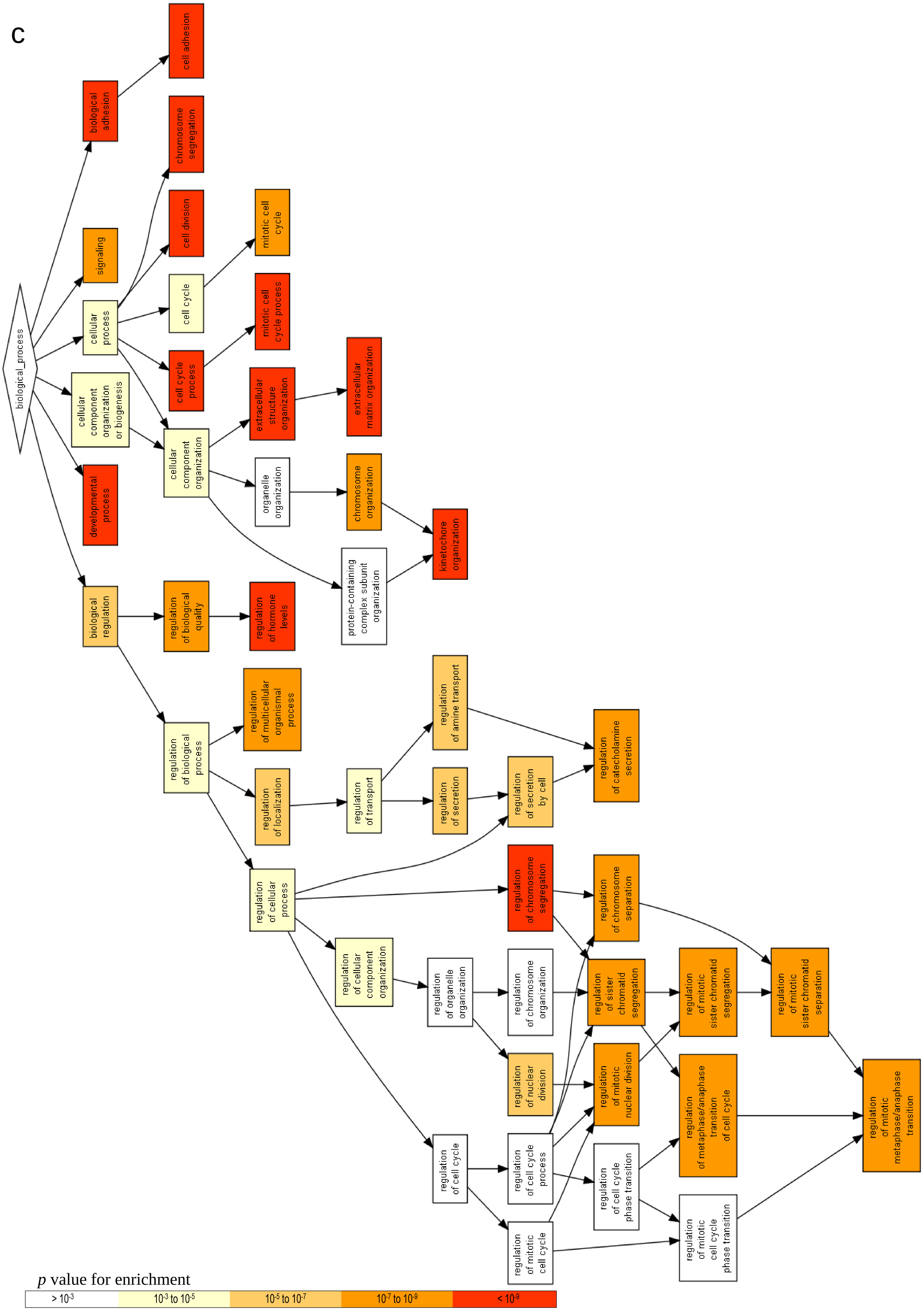
ESM Figure 2 Fetuin-A and SB431542 inhibit TGFBR-SMAD2/3 signalling and NICCs maturation. (a) RNAseq-based heat map showing common genes altered (1> Log_2FC < -1) by fetuin-A and SB431542 in NICCs maturated for 5d in medium containing fetuin-A (Fet-A/d5 vs HSA/d5) or HSA + SB (SB/d5 vs HSA/d5)

b



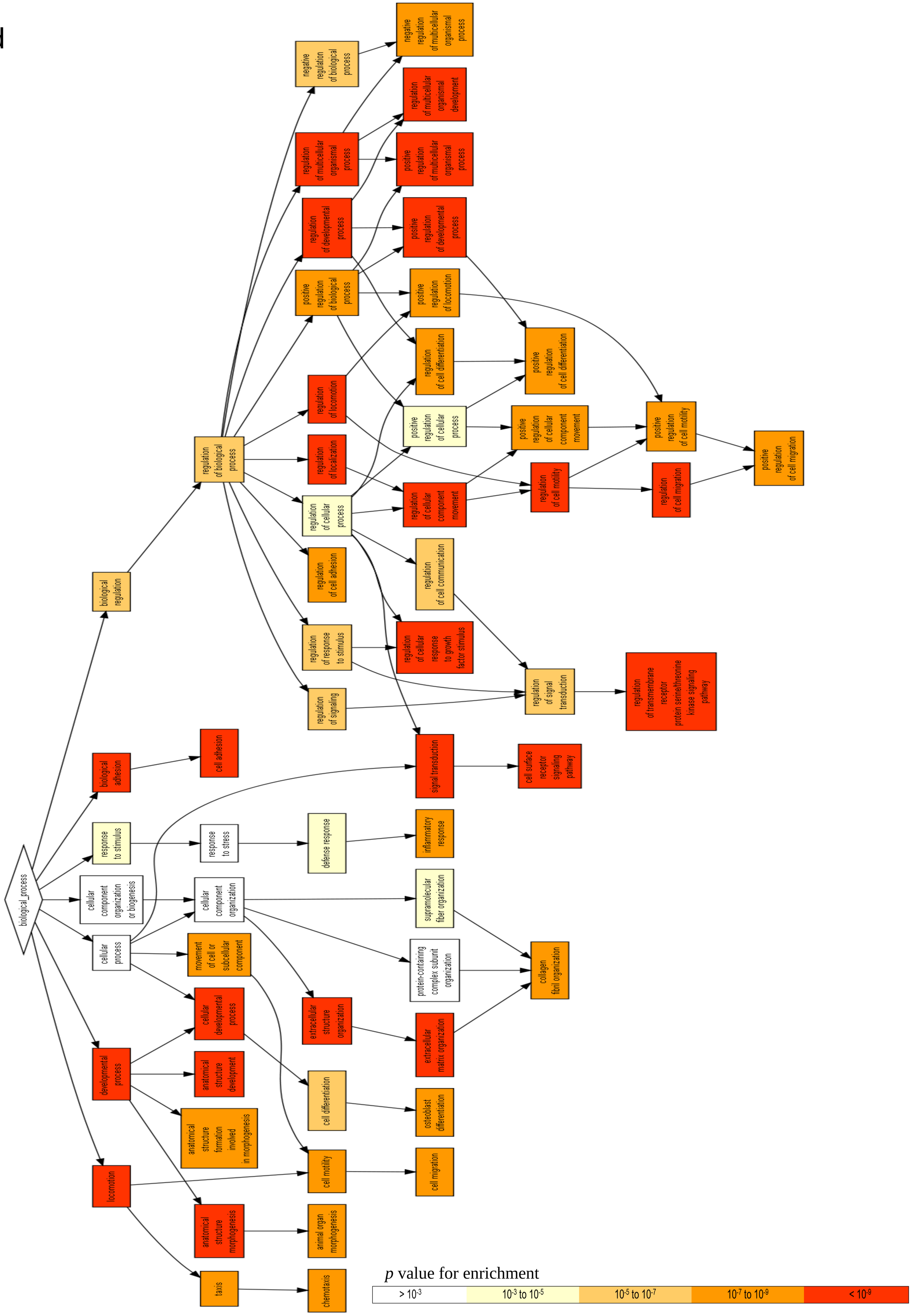
ESM Figure 2 Fetuin-A and SB431542 inhibit TGFBR-SMAD2/3 signalling and NICCs maturation. (b) Ranking of GO terms significantly enriched in DEGs upregulated in NICCs upon maturation in standard medium. False Discovery Rate < 2.

C

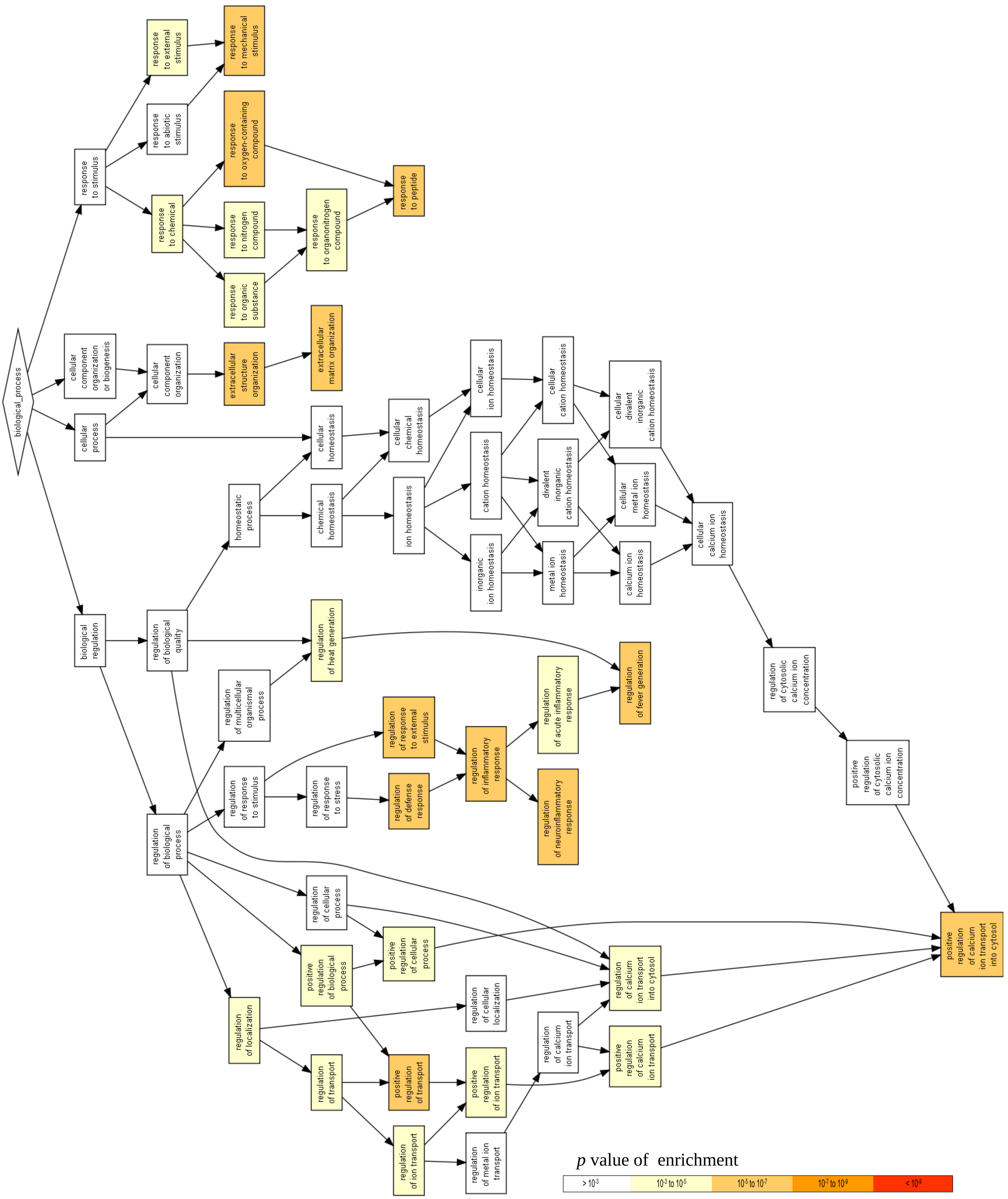


ESM Figure 2 Fetuin-A and SB431542 inhibit TGFBR-SMAD2/3 signalling and NICCs maturation. (c) Ranking of GO terms significantly enriched in DEGs downregulated in NICCs cultured in fetuin-A containing medium. False Discovery Rate < 2.

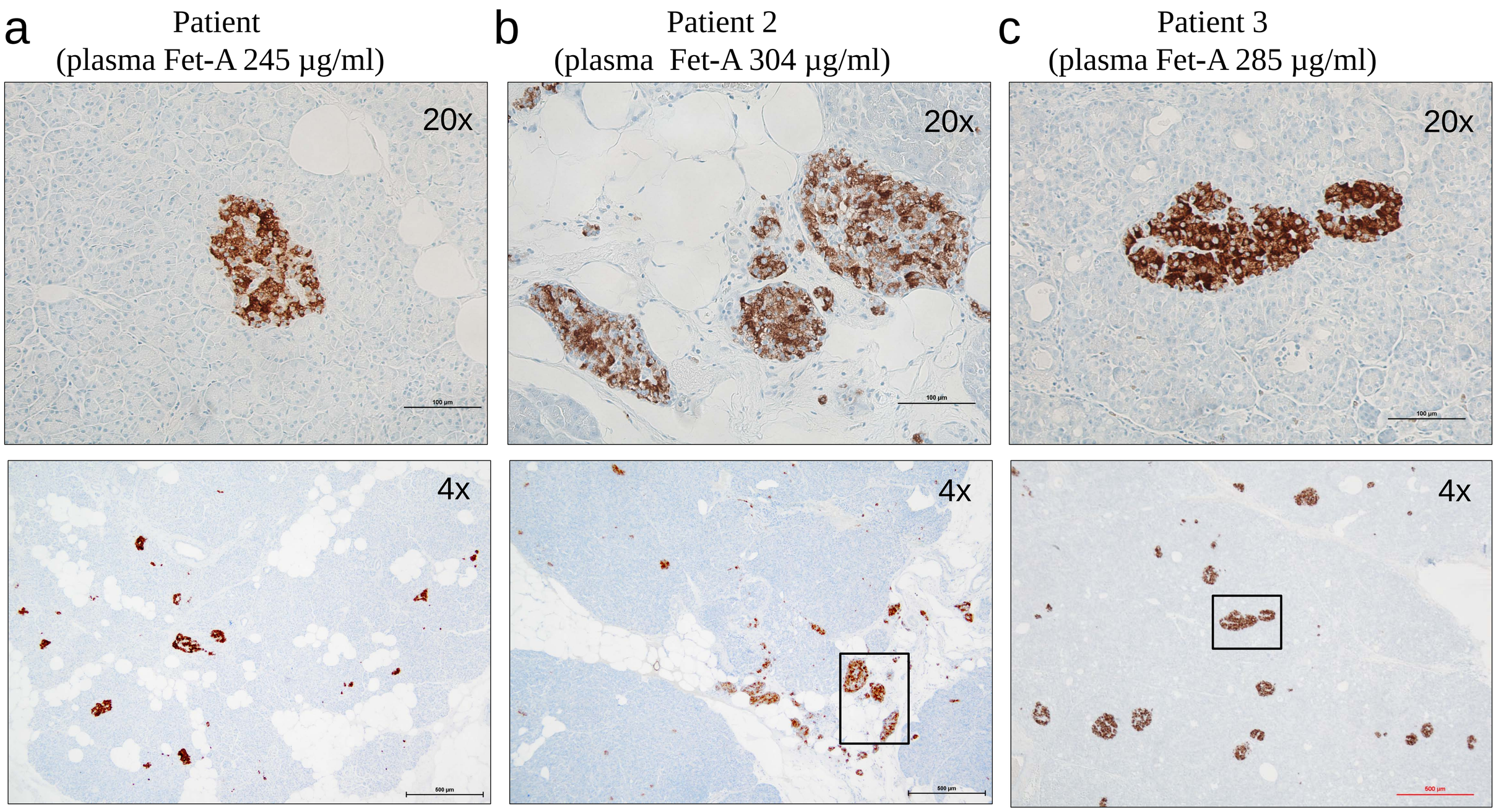
d



ESM Figure 2 Fetuin-A and SB431542 inhibit TGFBR-SMAD2/3 signalling and NICCs maturation. (d) Ranking of GO terms significantly enriched in DEGs downregulated in NICCs upon culture in HSA+SB-containing medium; False Discovery Rate < 2.



ESM Figure 3 Fetuin-A inhibits funtional maturation of adult human islets. Ranking of GO terms significantly enriched in genes altered in human islets following 2d culture in the presence of fetuin-A. False Discovery Rate < 2.



ESM Figure 4 Human pancreatic islet morphology and elevated fetuin-A levels. Representative microscopy images of human pancreatic sections from (a-c) n = 3 patients with plasma fetuin-A levels < 400 µg/ml and (d-f) n = 3 patients with plasma fetuin-A levels > 400 µg/ml; the pancreatic sections were stained for insulin (brown) and hematoxylin was used as counter-staining. Upper panels: 20x and lower panels: 4x magnifications.