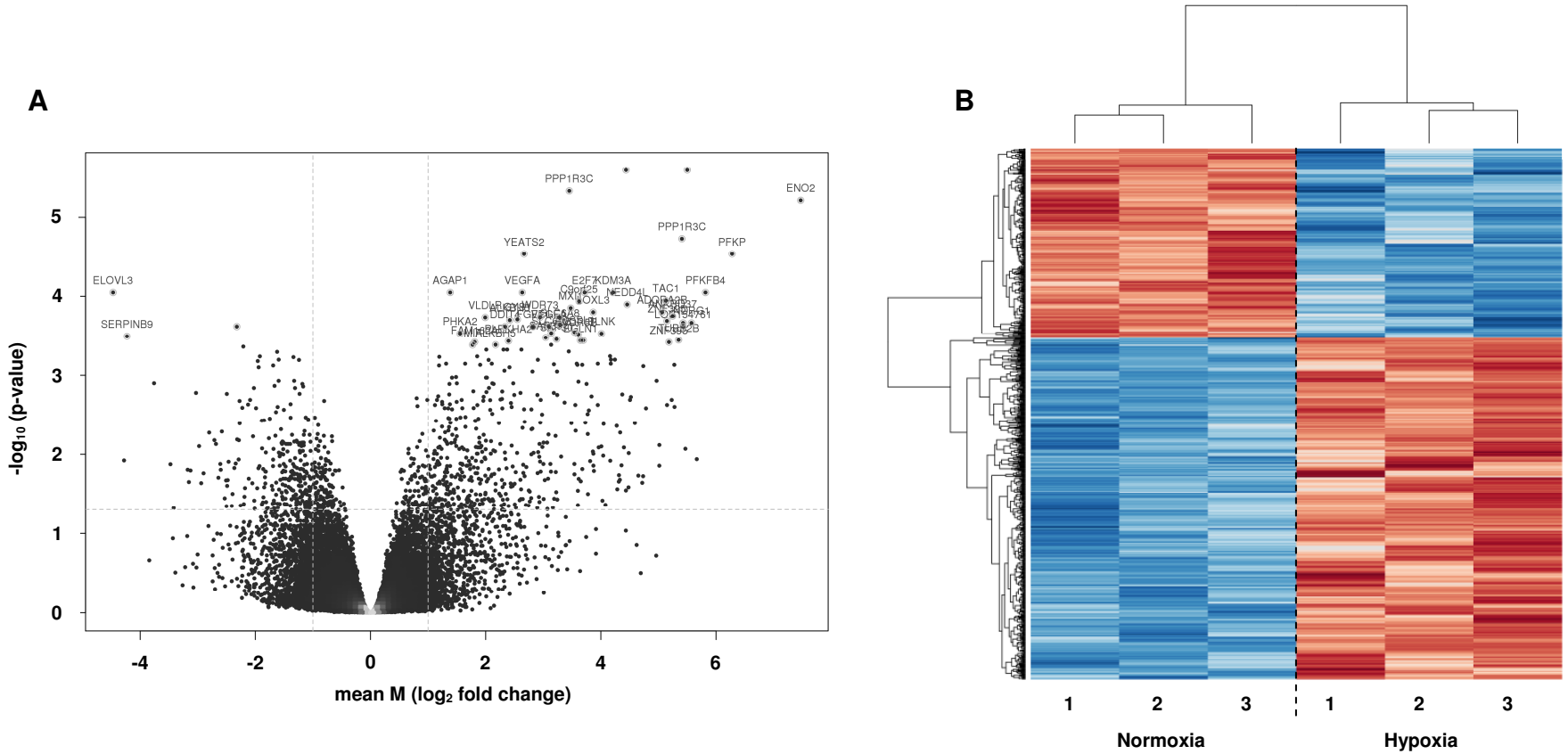
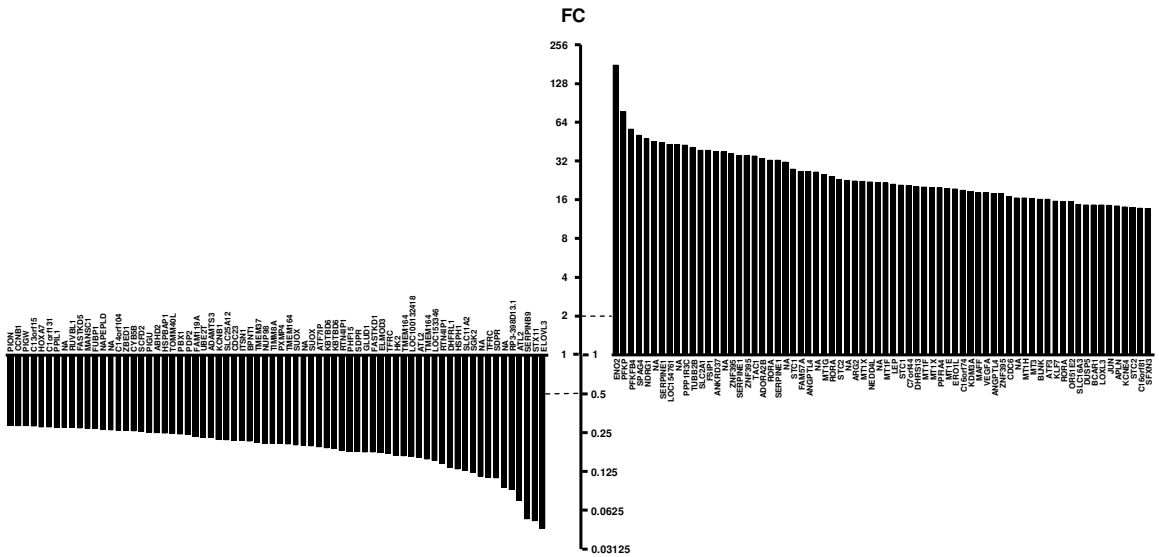


Suppl. 1: Volcano plot and clustering heat map analysis of 757 differentially regulated probe sets. A) The scatter plot represents all tested probe sets with their statistical significance of differential expression as -log10 of p-value (y-axis) and their extend of differential expression between normoxia and hypoxia as log2 fold change (x-axis). The horizontal dashed line separates probe sets according to their p-values (0.05) and the vertical dashed lines according to their mean M = log2 fold change (-1; +1). **B)** The heat map reflects gene expression values in normoxia vs. hypoxia. The colour intensity of single probes stands for their normalized expression, where blue represents low and red high expression respectively. Each column (1-3) represents one separate experiment, each row one of the 757 probe sets.



Suppl. 2: Probe set overview. The plot represents the top 70 up- and downregulated probe sets, referred to as their corresponding gene symbols, starting from the extreme fold change (FC) values of 177 and 0.045 respectively.

↑ set	Gene symbol	BHp	FC
1.	ENO2	6,12E-06	177,28
2.	PFKP	2,92E-05	77,66
3.	PFKFB4	8,95E-05	56,37
4.	SPAG4	1,15E-02	50,76
5.	NDRG1	2,16E-04	47,62
6.	LOC154761	2,40E-04	43,04
7.	TUBB2B	3,59E-04	40,79
8.	FSIP1	7,39E-04	38,73
9.	ANKRD37	1,77E-04	37,94
10.	SERPINE1	8,26E-03	37,36
11.	TAC1	1,13E-04	35,01
12.	ADORA2B	1,59E-04	33,44
13.	FBXO16	1,17E-03	31,30
14.	PPP1R3C	1,16E-05	26,69
15.	FAM57A	7,66E-04	26,66
16.	MT1G	1,85E-02	25,12
17.	ZNF395	7,31E-04	24,27
18.	SLC2A1	7,42E-03	23,26
19.	ARG2	9,65E-03	22,38
20.	ANGPTL4	1,54E-02	22,26
21.	LEP	8,18E-03	21,12
22.	MT1X	2,21E-02	21,11
23.	MT1F	2,47E-02	20,87
24.	C7orf44	1,37E-02	20,51
25.	DHRS13	5,31E-03	20,18
26.	PPFIA4	2,20E-02	19,86
27.	MT1E	2,75E-02	19,50
28.	STC1	7,01E-03	19,18
29.	RORA	1,14E-02	19,17
30.	C16orf74	6,36E-04	18,95
31.	KDM3A	8,95E-05	18,52
32.	STC2	2,32E-03	18,40
33.	MT1H	1,04E-02	16,46
34.	MT3	3,83E-02	16,31
35.	BLNK	2,95E-04	16,11
36.	ATF3	7,94E-03	16,09
37.	OR51F2	2,36E-03	15,42
38.	MAFF	6,87E-04	15,07
39.	SLC16A3	1,62E-02	14,72
40.	DUSP5	1,39E-02	14,63
41.	BCAR1	9,82E-03	14,62
42.	LOXL3	1,59E-04	14,59
43.	APLN	1,84E-03	14,30
44.	CDC6	3,06E-02	14,28
45.	C16orf81	3,17E-02	13,70
46.	MT2A	3,08E-03	13,64
47.	RAB33A	1,28E-03	13,47
48.	ERO1L	2,50E-03	13,43
49.	E2F7	8,95E-05	13,16
50.	NEDD4L	6,47E-03	12,85

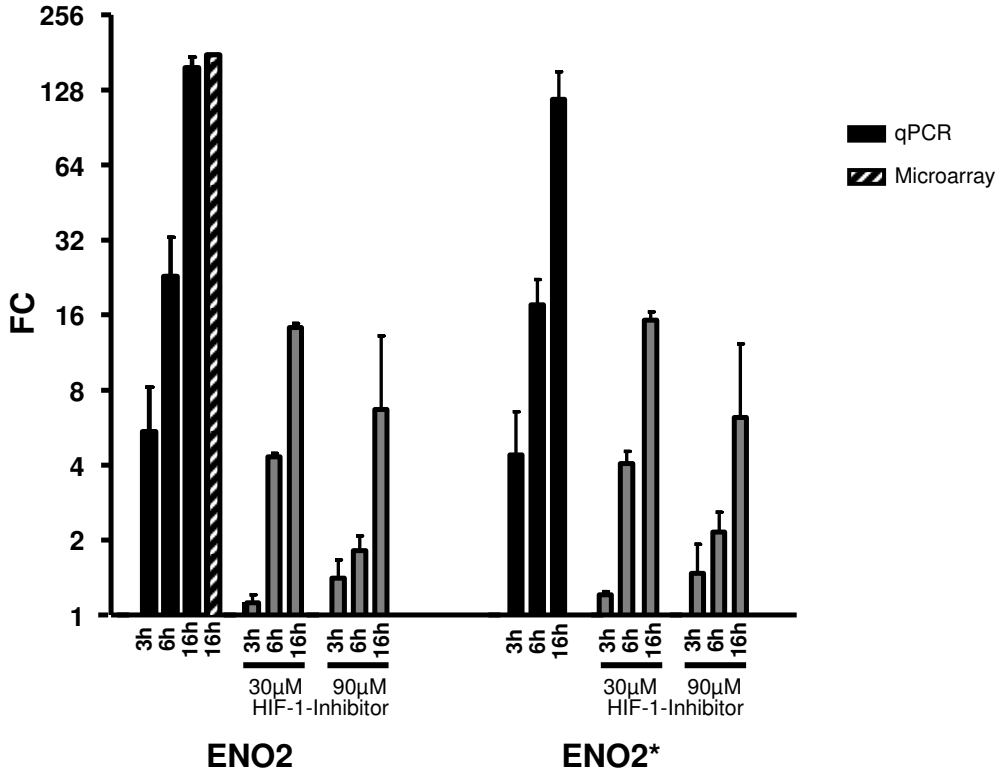
↑ set	Gene symbol	BHp	FC
51.	RNF19B	2,19E-02	12,56
52.	SFXN3	4,79E-03	12,45
53.	C9orf25	1,15E-04	12,31
54.	MT1P2	2,04E-02	12,25
55.	FUT11	1,20E-03	12,22
56.	WDR5B	3,02E-04	12,20
57.	SLC2A3	2,87E-02	12,13
58.	LIPG	4,38E-02	12,13
59.	PLA2G6	7,39E-04	12,07
60.	TMEM184B	7,39E-04	12,07
61.	TET1	2,36E-03	11,77
62.	KLF7	1,44E-02	11,72
63.	ADSSL1	2,84E-04	11,67
64.	AKAP13	1,32E-02	11,64
65.	VEGFA	1,52E-03	11,15
66.	MXI1	1,41E-04	11,13
67.	JUN	2,16E-02	10,71
68.	TRIB3	1,07E-02	9,92
69.	MGAT5	1,84E-04	9,69
70.	DOK5	3,71E-02	9,47
71.	INSIG2	5,86E-03	9,28
72.	TBC1D8	1,66E-03	9,08
73.	FOSL2	2,22E-03	8,91
74.	KCNE4	1,62E-02	8,87
75.	SAP30	3,41E-04	8,81
76.	SLC6A8	8,82E-04	8,74
77.	EGLN1	1,05E-03	8,61
78.	FLJ41603	4,91E-02	8,40
79.	RAB20	2,11E-02	8,15
80.	JAM2	3,65E-02	8,04
81.	SLC7A5	7,13E-03	8,03
82.	INHBE	1,32E-02	8,01
83.	P4HA2	2,04E-03	7,76
84.	RFX2	3,98E-03	7,72
85.	WDR73	1,84E-04	7,69
86.	FANCE	7,41E-03	7,64
87.	PLOD2	3,99E-02	7,64
88.	PNMA2	9,40E-03	7,52
89.	FLNB	4,33E-03	7,46
90.	HMOX1	4,76E-02	7,44
91.	MAPK7	1,21E-02	7,34
92.	MYO10	1,83E-02	7,32
93.	MTP18	9,59E-03	7,12
94.	FGF11	2,40E-04	7,06
95.	IL15	4,44E-02	6,70
96.	C9orf30	2,47E-02	6,47
97.	TMEFF1	2,47E-02	6,47
98.	METRNL	3,87E-03	6,39
99.	KBTBD9	1,88E-02	6,39
100.	HTRA3	2,68E-03	6,35

↑ set	Gene symbol	BHp	FC
101.	YEATS2	2,92E-05	6,35
102.	PHLDA1	2,43E-02	6,34
103.	LPCAT1	1,35E-02	6,28
104.	TGIF1	4,62E-03	6,23
105.	FLJ35024	2,75E-02	6,13
106.	EFNB2	3,65E-02	6,11
107.	PPP1R15A	3,77E-02	6,02
108.	RAB27A	2,99E-02	5,96
109.	LOX	2,26E-02	5,92
110.	GYS1	1,95E-04	5,86
111.	GTPBP2	9,62E-03	5,84
112.	PDE4C	1,28E-03	5,81
113.	PTGS2	4,73E-02	5,75
114.	DDIT4L	4,28E-02	5,68
115.	ALDOC	1,26E-03	5,57
116.	ETS1	1,42E-02	5,53
117.	PLEKHA2	1,07E-03	5,45
118.	MGC42105	2,55E-02	5,43
119.	NXN	2,23E-03	5,42
120.	PPP2R5B	2,32E-02	5,40
121.	ETV5	1,26E-02	5,33
122.	SHB	7,93E-04	5,33
123.	CLEC4C	3,67E-02	5,19
124.	SAMD4A	1,50E-02	5,14
125.	ARSJ	3,14E-02	5,09
126.	PDK3	8,06E-04	5,07
127.	PANX1	1,15E-02	5,07
128.	DDIT4	2,40E-04	5,06
129.	SCAI	9,52E-03	5,04
130.	AMPD3	4,25E-02	4,99
131.	WDR54	4,75E-04	4,96
132.	FAM13A	2,28E-02	4,94
133.	ALKBH5	3,06E-04	4,92
134.	CAMTA2	3,72E-02	4,92
135.	PTGES	4,96E-02	4,91
136.	LGALS3	2,58E-02	4,90
137.	ARAP1	2,29E-03	4,88
138.	MTSS1	2,10E-02	4,86
139.	CNOT8	1,94E-03	4,82
140.	AGAP1	2,42E-03	4,81
141.	RASSF5	7,41E-03	4,77
142.	SCARB1	8,37E-03	4,74
143.	RNF24	7,50E-03	4,73
144.	SIK1	1,55E-02	4,69
145.	SLC16A1	8,54E-03	4,69
146.	FAM26F	3,28E-02	4,61
147.	C4orf47	2,07E-02	4,58
148.	C3orf58	2,35E-02	4,51
149.	MAP3K8	2,85E-02	4,50
150.	DUSP3	1,47E-02	4,49

↓ set	Gene symbol	BHp	FC
1.	ELOVL3	8,95E-05	0,05
2.	STX11	1,19E-02	0,05
3.	SERPINB9	3,21E-04	0,05
4.	ATL2	1,05E-02	0,12
5.	SGK2	1,66E-03	0,12
6.	HSPH1	2,30E-02	0,13
7.	DHFRL1	1,73E-02	0,13
8.	DHFRP1	1,73E-02	0,13
9.	TFRC	2,91E-02	0,14
10.	SDPR	2,03E-02	0,14
11.	LOC153346	6,64E-03	0,15
12.	RTN4IP1	8,86E-03	0,16
13.	LOC100132418	1,32E-02	0,16
14.	HK2	5,16E-03	0,17
15.	TMEM164	1,16E-02	0,17
16.	ELMOD3	2,13E-02	0,18
17.	FASTKD1	4,53E-02	0,18
18.	GLUD1	1,71E-03	0,18
19.	GLUD2	1,71E-03	0,18
20.	PHF15	2,11E-02	0,18
21.	KBTBD6	3,83E-02	0,19
22.	ATF7IP	1,49E-02	0,19
23.	RP3-398D13.1	2,06E-02	0,20
24.	SUOX	9,77E-03	0,20
25.	PXMP4	6,65E-03	0,21
26.	TIMM8A	2,10E-03	0,21
27.	NUP98	4,06E-03	0,21
28.	TMEM37	4,44E-02	0,21
29.	BPNT1	2,56E-03	0,21
30.	CDC23	4,24E-02	0,22
31.	SLC25A12	3,42E-02	0,22
32.	KCNB1	2,66E-02	0,22
33.	ADAMTS3	2,33E-03	0,23
34.	UBE2T	2,02E-02	0,23
35.	SLC11A2	7,54E-03	0,23
36.	PDP2	2,31E-02	0,24
37.	TOMM40L	1,45E-03	0,25
38.	HSPBAP1	3,83E-02	0,25
39.	PIGU	2,59E-03	0,25
40.	ZBED1	1,49E-02	0,26
41.	C14orf104	7,93E-04	0,26
42.	NAPEPLD	5,77E-04	0,26
43.	FUBP1	3,74E-03	0,27
44.	MANSC1	4,26E-02	0,27
45.	FASTKD5	8,41E-03	0,27
46.	RUVBL1	4,03E-02	0,27
47.	PPIL1	3,47E-02	0,28
48.	SCFD2	1,51E-02	0,28
49.	PBX1	7,24E-03	0,28
50.	C1orf131	3,71E-03	0,28

Suppl. 3: The top 150 up- and top 50 downregulated genes in SGBS adipocytes after 16h of hypoxia. Members of the upregulated (↑) as well as downregulated (↓) gene set were ranked according to the genes´ FC. P-values (BHp) have been calculated according to Benjamini and Hochberg.

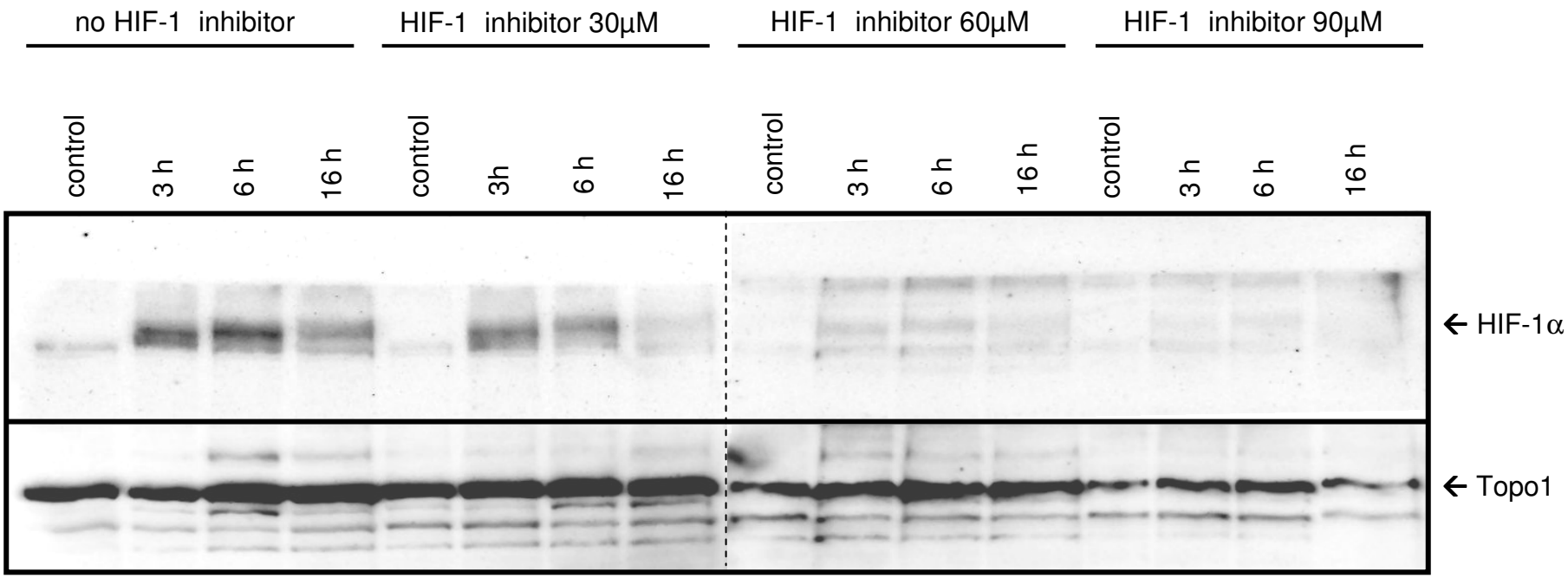
Following sequences for the primers were used:
ENO2: fwd 5'-AGGACACATTCATTGCTGAC-3' and rev 5'-CCCAGCTCTTCCTCAATTC-3', binding exons 10 to 12, and as a control (ENO2*) fwd 5'-CATGTGGCTGTAGATCCCAAG-3' and rev 5'-ACGCAGGCTTCAGTGAGTACAC-3', binding in exon 12, PFKP: fwd 5'-CGATGATTCCATTTGTGTGC-3' and rev 5'-AGCTTGAGCCACCACTGTTC-3',
PFKFB4: fwd 5'-CTCCTGTGGCATATGGTTG--3' and rev 5'-AGGTCTTGAGATGTCCACG 3',
ALDOC: fwd 5'-CTGCCACTGAGGAGTTCATC-3' and rev 5'-CTCCACCATCTTCTCCACTG-3',
TBP: fwd 5'-GGGAGCTGTGATGTGAAGTTT-3' and rev 5'-AAGGAGAACAATTCTGGGTTTG-3',
ATF3: fwd 5'-GTCTCTGCCTCGGAAGTGAG-3' and rev 5'-.TGACAAAGGGCGTCAGGT-3',
JUN: fwd 5'-ACAGAGCATGACCCTGAACC-3' and rev 5'-CGTTGCTGGACTGGATTATCA-3',
FOSL2: fwd: 5'-CGGATCATGTACCAGGATTA-3' and rev TGAGCCAGGCATATCTACC-3', and
KLF7: fwd 5'-CTTCTCAGCTTTACCATCCCTG-3' and rev 5'-GGAAGCGTGGAGGAAACAG-3'.



Suppl. 4: Primer sequences and alternate qPCR data for ENO2. QPCR primers were specific for ENO2, not for ENO1 due to six mismatches. There was a distinct melting curve and no second product detectable. Nevertheless, we repeated the qPCR with a second primer pair (ENO2*) binding the same sequence parts as used by the affymetrix probe set 201313_at for ENO2 and which does not bind ENO1. The results of both qPCRs were comparable.

Immunoblotting

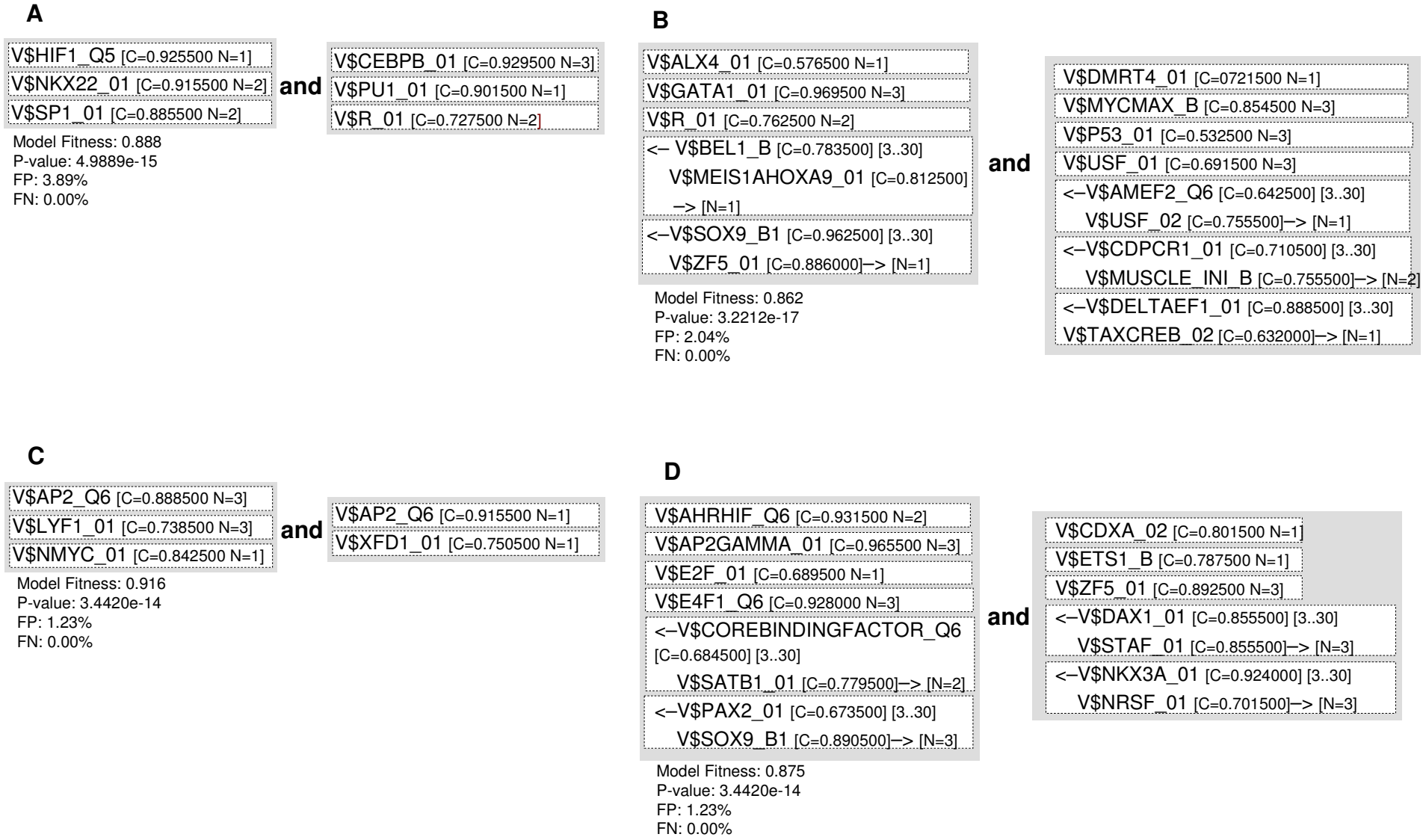
For preparation of nuclear SGBS extracts, NE-PER® Nuclear and Cytoplasmic Extraction Reagents (Pierce Biotechnology, IL, USA) containing a protease inhibitor cocktail and a phosphatase inhibitor cocktail were used. Total protein concentration was determined using the protein assay reagent (Bio-Rad Laboratories, Munich, Germany). Extracts were dissolved in 4x SSB loading buffer containing 20% β-mercaptoethanol and boiled. Fifteen micrograms of nuclear extracts were separated by SDS-PAGE electrophoresis and then transferred to nitrocellulose membrane (Schleicher & Schuell, Dassel, Germany). Membranes were blocked and incubated with primary antibodies specific for HIF-1α (R&D Systems, MN, USA) and Topoisomerase I (Cell Signaling, Frankfurt, Germany), washed and then incubated with horseradish-peroxidase-conjugated anti-mouse and anti-rabbit secondary antibodies (GE Healthcare, Buckinghamshire, UK), respectively. Specific bands were visualized by enhanced chemiluminescence reagent (ECL Plus; GE Healthcare) and analyzed in an AutoChemi detection system (UVP, Cambridge, UK).



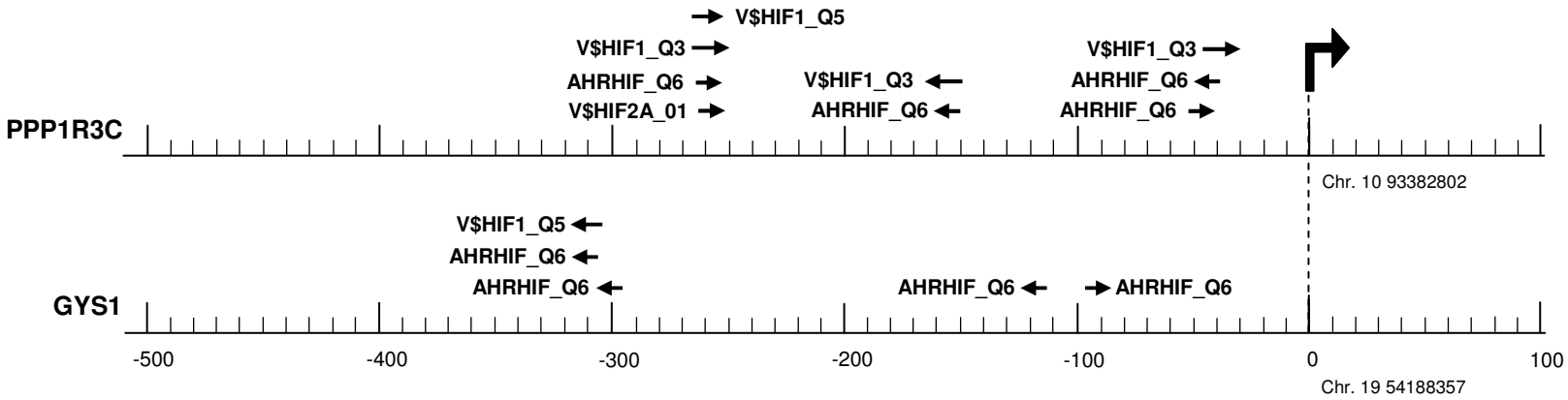
Suppl. 5: Effect of HIF-1a Inhibitor on protein levels in SGBS adipocytes under hypoxic cultivation. Fully differentiated SGBS adipocytes were incubated under hypoxic (1% O2) or under normoxic conditions in presence of indicated concentrations of the HIF-1 a inhibitor CAY10585 for up to 16h. Protein levels of HIF-1a and topoisomerase 1 (Topo1) as a control were examined by immunoblotting.

		Matrix sequence	Matrix name	Gene symbol	Yes/No	P-value	Positions	Matrix match	Matched sequence
ENO2	1.		*V$AP1_01*	FOS; FOSB; FOSL1,-2; JUN; JUNB, -D	inf	2.00E-03	-131(-)	0.986	tccTGACTcatcg
	2.		*V$AP1_Q2_01*	FOS; FOSB; FOSL1, -2; JUN; JUNB, -D	inf	2.00E-03	-127(+)	1.000	TGACTcatcggg
	3.		*V$AP1_C*	ATF2; FOS; FOSB; FOSL1, -2; JUN; JUNB, -D; SMAD3; TGIF1	inf	2.00E-03	-128(-)	1.000	cTGACTcat
	4.		*V$NF1_Q6*	NFIC	489.00	4.10E-03	-493(+)	0.990	cgtgggtgagaGCCAAga
	5.		*V$NF1_Q6_01*	NFIC	244.50	6.10E-03	-493(+)	0.992	gtgggtgagaGCCAAga
	6.		*V$E2_Q6_01*	n/a	195.60	8.69E-05	-181(-)	0.917	caccctcgtCGGTCcc
							-183(+)	0.918	tcCACCCtcgtcggtc
	7.		*V$HIF1_Q5*	HIF1A	163.00	8.10E-03	-154(+)	0.967	cgtACGTGcgcc
	8.		*V$BACH1_01*	BACH1, -2	163.00	8.10E-03	-131(-)	0.936	ctcctgACTCAtcgg
	9.		*V$E2_Q6*	n/a	163.00	8.10E-03	-182(+)	0.965	ccacccLcgLCGGTCc
	10.		*V$HIF2A_01*	EPAS1	163.00	8.10E-03	-153(+)	0.997	gtACGTGcgc
	11.		*V$E2_01*	n/a	75.23	4.30E-04	-182(+)	0.958	ccaccctcgtCGGTCc
							-182(-)	0.925	cCACCCtcgtcggtcc
PFKP	1.		*V$HIF1_Q5*	HIF1A	244.50	6.10E-03	514(+)	0.987	cggACGTGcggc
	2.		*V$HIF1_Q3*	HIF1A	244.50	6.10E-03	513(+)	0.975	ccggACGTGcggct
	3.		*V$MYOD_Q6_01*	ARID5B; ASCL1; MYF5; MYF6; MYOD1; MYOG; TCF12, -3, -4	163.00	8.10E-03	130(-)	0.976	ctgccccACCTGtggcgc
PFKFB4	1.		*V$AP4_01*	TFAP4	inf	2.00E-03	240(-)	0.949	gggaccccAGCTGtttct
	2.		*V$TFE_Q6*	MITF; TFE3; TFEB, -C	489.00	4.10E-03	366(-)	1.000	tcACATGa
	3.		*V$YY1_01*	YY1	489.00	4.10E-03	81(+)	0.992	ggagGCCATttttgaag
	4.		*V$BACH1_01*	BACH1, -2	244.50	6.10E-03	256(+)	0.943	ctgaTGAGTcacact
	5.		*V$STAT_Q6*	STAT1, -2, -3, -4, -5A, -5B, -6	244.50	6.10E-03	569(-)	0.994	tccCAGAAtggtg
	6.		*V$PAX6_Q2*	PAX6	244.50	6.10E-03	276(-)	0.852	aagTTCCAggtctt
	7.		*V$NRF2_Q4*	BACH1, -2, MAF; MAFB, -F, -G, -K; NFE2; NFE2L1, -2, -3	163.00	8.10E-03	256(+)	0.945	ctgatgAGTCAca
	8.		*V$AP2ALPHA_03*	TFAP2A, -B, -C	97.80	2.71E-04	436(+)	0.936	ggagcctgAGGCCta
							436(-)	0.936	ggAGCCTgaggccta
	9.		*V$AP1_01*	FOS; FOSB; FOSL1, -2; JUN; JUNB, -D	69.86	4.90E-04	257(+)	0.970	tgatgAGTCAcac
							257(-)	0.961	tgaTGAGTcacac
	10.		*V$AP1_C*	ATF2; FOS; FOSB; FOSL1, -2; JUN; JUNB, -D; SMAD3; TGIF1	48.90	9.36E-04	259(+)	0.985	atgAGTCAc
								0.979	aTGAGTcac
	11.		*V$AP2ALPHA_02*	TFAP2A, -B, -C	37.62	1.50E-03	436(+)	0.953	ggAGCCTgaggccta
							436(-)	0.952	ggagcctgAGGCCta
	12.		*V$STAT5B_01*	STAT1, -2, -3, -4, -5A, -5B, -6	27.17	2.80E-03	565(+)	0.905	agCTTCCcagaatgg
							565(-)	0.939	agcttcccAGAATgg
	13.		*V$HSF1_01*	HSF1, -2	26.43	2.90E-03	273(+)	0.990	AGAAAgttcc
							273(-)	0.966	agaaaGTTCC
	14.		*V$HSF2_01*	HSF1, -2	23.85	3.60E-03	273(+)	0.986	AGAAAgttcc
							273(-)	0.993	agaaaGTTCC
ALDOC	1.		*V$IPF1_Q4*	PDX1	inf	2.00E-03	124(-)	0.969	gttCATTActtc
	2.		*V$ARNT_01*	ARNT	inf	2.00E-03	252(-)	0.985	cccggCACGTggtaaa
	3.		*V$CMYC_02*	MAX: MYC; MYCN	489.00	4.10E-03	254(-)	0.975	cggcACGTGgta
	4.		*V$NMYC_01*	MAX; MYC; MYCN	489.00	4.10E-03	254(-)	0.998	cggCACGTggta
	5.		*V$TEL2_Q6*	ELF1, -2; ELK1, -4; ERG; ETS1, -2; ETV7; FLI1	489.00	4.10E-03	129(+)	1.000	ttACTTCctg

Suppl. 6: Transcription factor binding sites identified within ENO2-, PFKP-, PFKFB4-, and ALDOC-promotors.
All sequences of matched PWMs within the cut-off-values as described in methods were ranked according to their “Yes/No” ratio (For ALDOC only top 5 of total 26 hits are displayed). The respective binding positions are indicated together with the matched sequence and the similarity score for the matrix match.



Suppl. 7: Promoter model calculated for the glycolysis and insulin pathway gene set. Two models were generated to fit glycolysis involved ENO2, PFKP, PFKFB4, ALDOC, GPI, HK1, HK2, MPI, PFKL, PGK1, and TPI1 genes. One consisting solely of single matrices (A), the other also integrates matrix pairs (B). Two further models were generated to fit insulin pathway involved CBL, CREB1, GRB10, GYS1, INSR, MAP2K1, MAPK7, and NEDD4L genes, comprising only single matrices (C) or also pairs (D). The models were generated by the composite model analysis (CMA) as described in methods part. For each of the four specifications, the one with highest model fitness is displayed. All models consist of 2 groups, connected with a Boolean operator, harboring different single- or pairs of PWMs with their matrix cut-offs [C], the distance in pair ([n..n]) and the number of matrix matches expected in the module [N]. Overall model fitness, p-values as well as false positive (FP) and false negative (FN) frequencies of the models are indicated.



Suppl. 8: Binding sites for HIF-family transcription factors within promoter regions of PPP1R3C and GYS1. Schematic representation of matched PWMs (arrows) within the proximal promoters, representing the position of transcription factor binding sites. Start point of transcription is marked by a dashed line, the genome positions are indicated.

Gene set	Gene symbol	Molecule name	BHp	FC
↑	SLC2A1	GLUT1	7.42E-03	23.26
↑	SLC16A3	MCT4	1.62E-02	14.72
↑	SLC2A3	GLUT3	2.87E-02	12.13
↑	SLC6A8	CT1	8.82E-04	8.74
↑	SLC7A5	LAT1	7.13E-03	8.03
↑	SLC16A1	MCT1	8.54E-03	4.69
↑	SLC39A14	ZIP14	1.15E-02	3.98
↑	SLC15A4	PHT1	4.02E-02	3.08
↑	SLC29A4	ENT4	4.08E-02	2.55
↑	SLC38A5	SN2	3.67E-02	2.20
↓	SLC25A12	ARALAR1	3.42E-02	0.22
↓	SLC11A2	NRAMP2	7.54E-03	0.23
↓	SLC19A3	THTR2	1.75E-02	0.40
↓	SLC35B4	n/a	3.42E-02	0.44

Suppl. 9: The top up- and top downregulated transporter genes in SGBS adipocytes after 16h of hypoxia. Members of the upregulated (↑) as well as downregulated (↓) genes for transporters of the solute carrier family (SLC) were ranked according to the genes´ FC. P-values (BHp) have been calculated according to Benjamini and Hochberg.