SUPPLEMENTARY INFORMATION

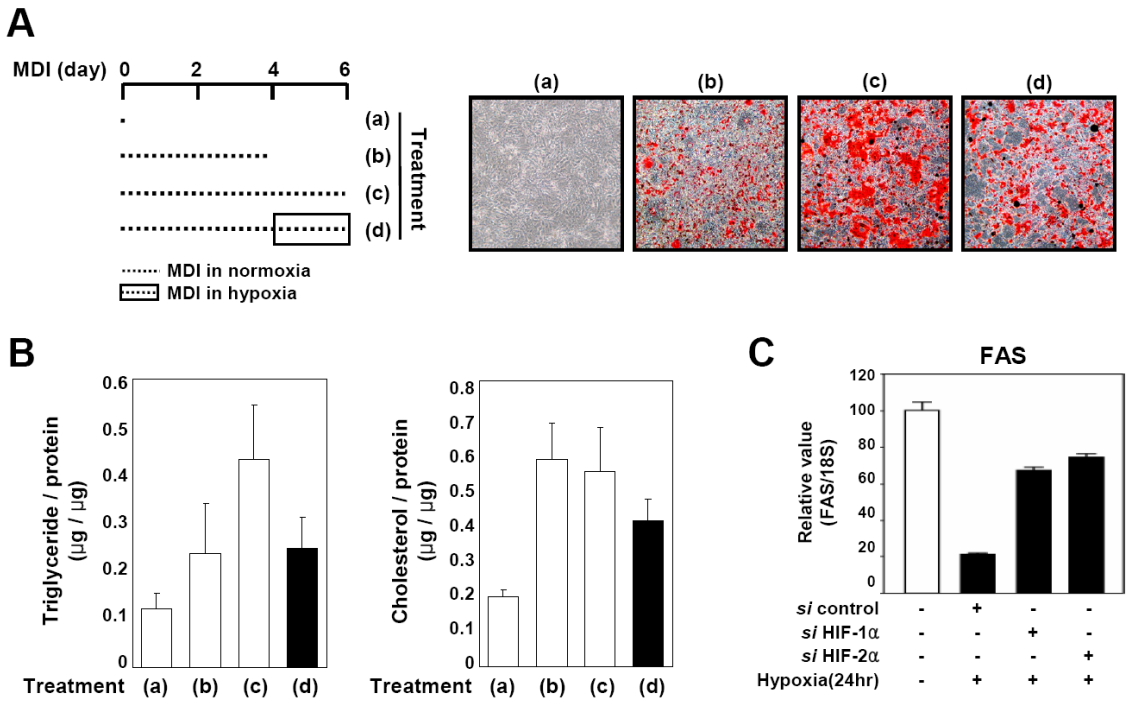

Figure S1. Effect of hypoxia on the lipid synthesis and FAS expression. (A) 3T3-L1 cells were plated at 1×10^5 cells in a 60 mm plate. At confluence, differentiation of 3T3-L1 preadipocytes was induced by DMEM containing 10 % fetal bovine serum and MDI (500 μM of 3-isobutyl-1-methylxanthine, 2 μM of dexamethasone, and 5 μg/ml of insulin) and maintained for the indicated days. After 4 day induction, the differentiated adipocytes were exposed to hypoxia (1% O_2, 48 hr) as indicated (left panel, (d)). Lipid droplets of mature adipocytes were stained with oil red O (0.5 % in isopropanol) as described (30). Microscopic images of oil red O-stained lipid droplets in the 3T3-L1 cells were visualized (right panel). (B) Effect of hypoxia on the lipid synthesis. Whole cell lysates were prepared and levels of triglyceride and cholesterol were measured according to the instructions of the manufacturer (Sigma Co.). (C) Effect of HIF-1α and HIF-2α on hypoxic-repression of FAS. Hepa1c1c7 cells were transfected with the indicated *si*RNAs as described. Before harvest, the transfected cells were exposed to hypoxia (1 % O_2, 24 h). We confirmed the specific reduction of HIF-1α and HIF-2α mRNA by the cognate *si*RNAs (Fig. 2D). The level of FAS mRNA was quantified by Q-PCR. The expression level of 18S rRNA was used for normalization. Values represent means and standard deviations of three experiments.

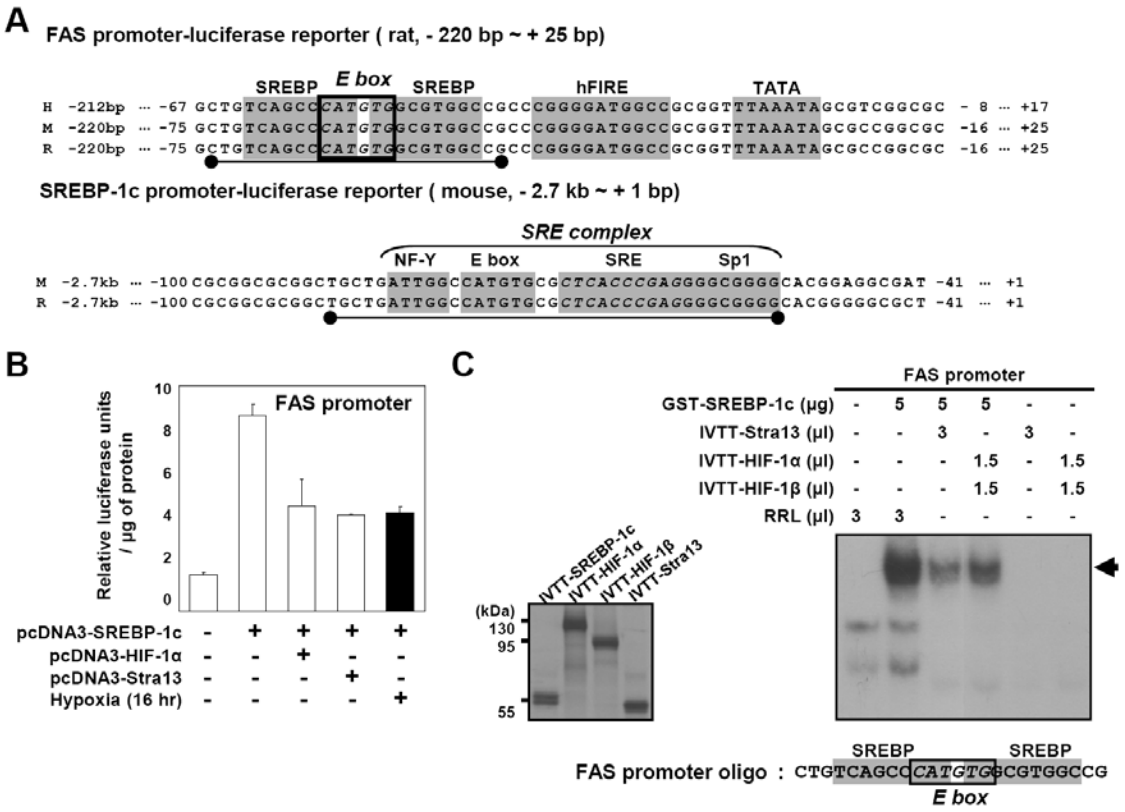

Figure S2. Effect of hypoxia on the FAS promoter activity. (A) Sequence comparison among human (indicated as 'H'), mouse (indicated as 'M') and rat (indicated as 'R') promoters of FAS or SREBP-1c genes. Boxed sequences indicate selected regulatory sequences: E-box consensus, hFIRE; hepatic FAS insulin response element, SREBP; SREBP-1c binding site flanked E-box, TATA-box, NF-Y; inverted CCAAT, Sp1 site; stimulatory protein 1 site, SRE; sterol regulatory element. (B) Effect of hypoxia on the FAS promoter activity. The rat FAS promoter-driven reporter plasmid (250 ng) and pCHO110 (50 ng) were transfected into 5 x 10^4 NIH 3T3 cells together with 250 ng of the indicated plasmid and luciferase assays were performed as described (26). Numbers represent averages and standard deviations of three independent experiments. (C) DNA binding activity of SREBP-1c on the FAS promoter. EMSAs were performed using the radiolabeled oligonucleotides for the FAS promoter (– 74 ~ – 51 bp of rat FAS gene) shown below. Recombinant GST-SREBP-1c protein was incubated with the indicated amount of either Stra13- or HIF-1α/HIF-1β-programmed rabbit reticulocyte lysate, followed by incubation with radiolabeled oligonucleotides. SREBP-1c, Stra13, HIF-1α, and HIF-1β were *in vitro*-transcribed and translated by using [^{35}S]-methionine and rabbit reticulocyte lysate. 1.5 μl among 15 μl of the programmed rabbit reticulocyte lysate was resolved by electrophoresis through 10 % SDS-PAGE and visualized by autoradiograph to confirm the expression of IVTT HIF-1α, -1β, SREBP-1c and Stra13 (left).

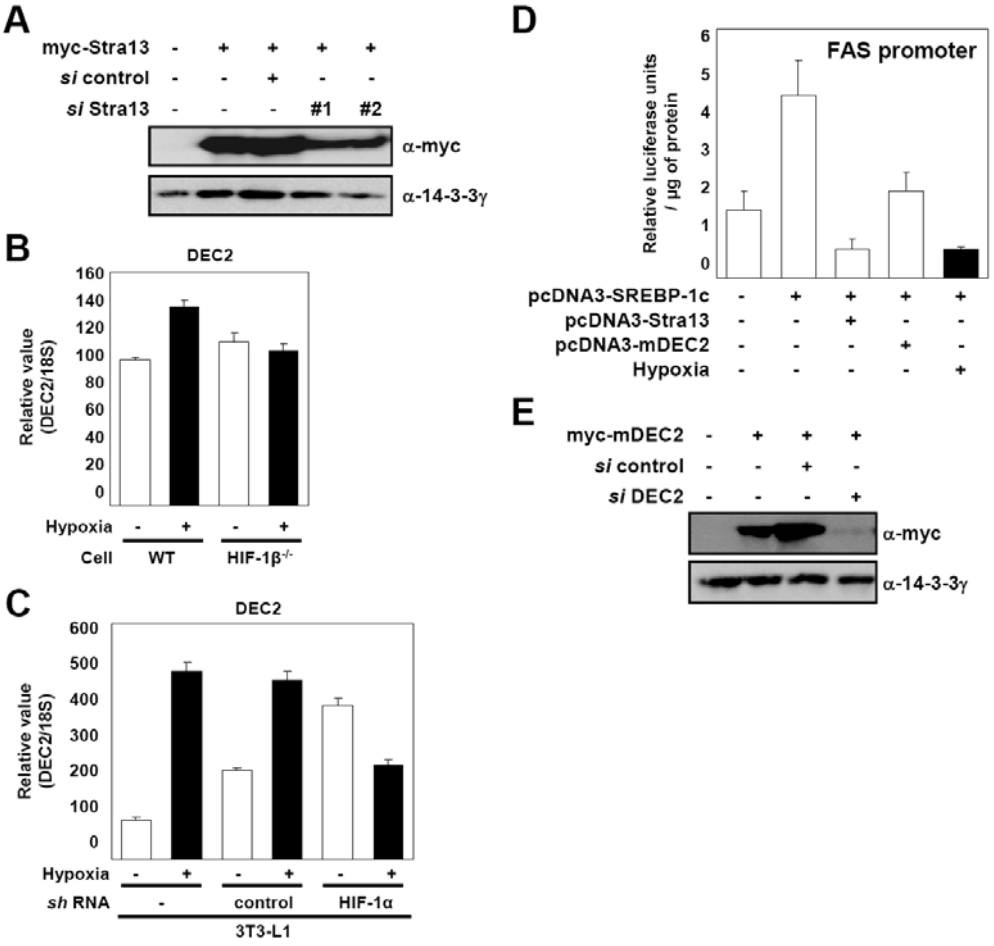

Figure S3. Effects of Stra13/DEC1 and DEC2 on the hypoxic repression of FAS promoter. (A) Effect of *si*RNA against Stra13 on the expression of the myc-Stra13 protein. In order to test whether the *si*RNA against Stra13 reduces the Stra13 protein as well as Stra13 mRNA (see Fig. 6A), we transfected both 300 pmole of *si*RNAs against Stra13 and 3 μg of pCMV-myc-Stra13 plasmid into 5×10^5 Hepa1c1c7 cells in a 60-mm plate using PolyMAG (Chemicell GmBH, Germany). 48 hours after transfection, immunoblot analysis was performed using anti-myc antibody and anti-14-3-3γ antibody. Western blot with anti-14-3-3γ antibody was used as a loading control. Bands were visualized by chemiluminescence. (B) (C) Effects of HIF-1α and HIF-1β on the expression of DEC2. The indicated cells were exposed to hypoxia for 16 hr. The levels of DEC2 mRNAs were detected by Q-PCR. The expression level of 18S rRNA was used for normalization. (D) Effect of DEC2 on the hypoxic repression of FAS promoter activity**.** The rat FAS promoter-driven reporter plasmid (250 ng) and pCHO110 (50 ng) was transfected into 5×10^4 NIH 3T3 cells together with 250 ng of the indicated plasmid. The transfected cells were incubated in hypoxia (1 % O_2, 16 h) before harvesting, and luciferase assays were performed (26). Numbers represent averages and standard deviations of three independent experiments. (E) Effect of *si*RNA against DEC2 on the expression of the myc-DEC2 protein. In order to test whether the *si*RNA against DEC2 reduces the DEC2 protein as well as DEC2 mRNA (see Fig. 8A), we transfected both 300 pmole of *si*RNAs against DEC2 and 3 μg of pCMV-myc-DEC2 plasmid into 5×10^5 Hepa1c1c7 cells in a 60-mm plate using PolyMAG (Chemicell GmBH, Germany). 48 hours after transfection, immunoblot analysis was performed using anti-myc antibody and anti-14-3-3γ antibody. Western blot with anti-14-3-3γ antibody was used as a loading control. Bands were visualized by chemiluminescence.

Table S1. Primers used for Q-PCR, RT-PCR and *si*RNA

Gene symbol	sense	antisense	Accession number
Primers used for Q-PCR and RT-PCR			
FAS	TGCTCCCAGCTGCAGGC	GCCCCGTAGCTCTGGGTGTA	X54671
SREBP-1c	CACTTCATCAAGGCAGACTC	CGGTAGCGCTTCTCAATGGC	AF286469
Stra13	TTGTCGGGAAGAAATCTCGAGGCA	AGTGTTCTCATGCTTCGCCAGGTA	NM_011498
Stra13 (full-length)	CATGGAACGGATCCCCAGC	GTCTTTGGTTTCTAAGTT	NM_011498
DEC2	AAAGCGCGCGAGGTATTGCAAGAC	ATTGCTTTACAGAATGGGGAGCG	NM_024469
HIF-1α	TCTCGGCGAAGCAAAGAGTCTGAA	TAGACCACCGGCATCCAGAAGTTT	AF003695
HIF-2α	AAGTGGCCTGTGGTTGATCAGAGT	CTGCCGCTTTAGCTTCAGCTTGTT	NM_010137
VEGF	CCATGAACTTTCTGCTGTCTT	ATCGCATCAGGGGCACACAG	AF022375
18S	ACCGCAGCTAGGAATAATGGAATA	CTTTCGCTCTGGTCCGTCTT	X03205
***si*RNA duplex sequences**			
HIF-1α	UGUGAGCUCACAUCUUGAU(dTdT)	AUCAAGAUGUGAGCUCACA(dTdT)	AF003695
HIF-2α	GCAACUACCUGUUCACCAA(dTdT)	UUGGUGAACAGGUAGUUGC(dTdT)	NM_010137
Stra13(#1)	GCACGUGAAAGCAUUGACA(dTdT)	UGUCAAUGCUUUCACGUGC(dTdT)	NM_011498
Stra13(#2)	GAACGUGUCAGCACAAUUA(dTdT)	UAAUUGUGCUGACA GUUC(dTdT)	NM_011498
DEC2	GCAUUUGGAGAAAGCAGUA(dTdT)	UACUGCUUUCUCCAAAUGC(dTdT)	NM_024469
Control (GFP)	GUUCAGCGUGUCCGGCGAG(dTdT)	CUCGCCGGACACGCUGAAC(dTdT)	

* An irrelavant control *si*RNA against GFP (Green Fluorescence Protein) was provided by Samchully Pharm. Co. (Seoul, Korea).

Table S2. Sequences for *sh*RNA

Gene symbol	sequence (5'-3')	Accession number
HIF-1α	GATCCG**TGTGAGCTCACATCTTGAT**TTCAAGAGA**ATCAAGATGTGAGCTCACA**TTTTTTAGATCTG	NM_010137
Control	GATCCG**TGCGTTGCAGTACCAAC**TTCAAGAGATTTTTTACGCGTG	*

* The sequence for an irrelavant control *sh*RNA was provided from BD Biosciences.
Bold letters indicate the target sequences and underlined letters indicate sequences for BamHI or EcoRI.

Table S3. Primers used for ChIP analyses

promoter	sense	antisense	region
FAS	CGGCGCGCCGGGTCCCGGGG	CCGCGGCCGGCGCTATTTAAA	– 135 ~ – 14
SREBP-1c	AGCGACCGGCCATAAACCAT	GGTTGGTACCACAGTGACCG	– 247 ~ + 56
Stra13	AACACGTGAGGCTCATGT	GTTAAATGGGAGCGAGTG	– 545 ~ – 410