Supplementary Table S1: Information for all human primary ASC lines employed in the present study.

ASC Number	Ethnicity	Gender	Phenotype
APOD-01	Malay	Male	Obese
APOD-02	Malay	Female	Obese

Supplementary Table S2: Information for all primary Wharton's jelly derived MSC isolates used in the present study.

MSC Number	Phenotype	Race	Gender	Gestational Period (weeks	Weight (g)
01	SGA	Chinese	Female	39	2420
23	SGA	Chinese	Female	37	2440
56	SGA	Indian	Female	37	2265
70	SGA	Indian	Female	37	2440
75	SGA	Indian	Female	37	2480
82	SGA	Indian	Male	38	2835
83	SGA	Chinese	Male	39	2695
84	SGA	Indian	Female	38	2615
85	SGA	Indian	Male	40	2515
18	Normal	Chinese	Female	40	3125
44	Normal	Chinese	Female	39	3130
31	Normal	Indian	Female	40	3070
50	Normal	Indian	Female	37	2935
57	Normal	Indian	Female	39	3275
60	Normal	Indian	Female	39	2905
64	Normal	Chinese	Female	40	3830

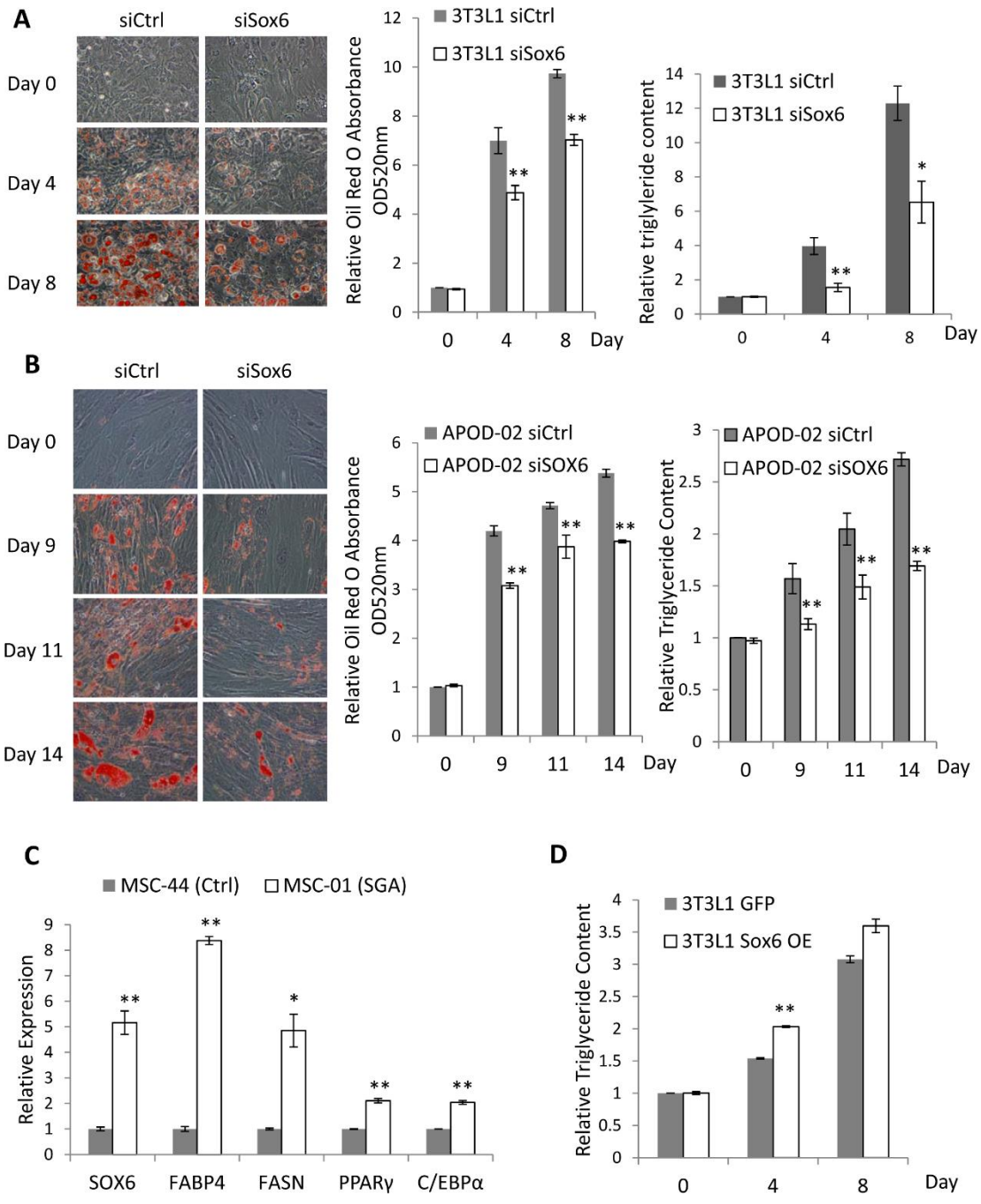
Supplementary Table S3: List and sequence of all oligonucleotides used in the present study.

Human mRNA Expression Primers		
Gene	**Forward Primer**	**Reverse Primer**
SOX6	GCGTTCTGTCATCTCAGCAAAG	TTTCGGAAGGAATATAGGGAACAT
SOX5	ACCTCAGGAGTTTGAAAGGATG	ACAAGTCTCTTGCGTCAGCA
SOX9	GCTCTGGAGACTTCTGAACGA	CCGTTCTTCACCGACTTCCT
SOX13	AAAGAAGTGGTGCCAGCCAT	AGCTCCTTCTCTGCTAGGCT
MEST	GCAGGATGAGGGAGTGGTG	GGGGTGAGACCTCGAGAGAA
ADIPOQ	CTGTTGCTGGGAGCTGTTCT	CCCTTAGGACCAATAAGACCTGG
PPARγ	GTGGCCGCAGAAATGACCA	GGAGATGCAGGCTCCACTTT
CEBPα	TGTATACCCCTGGTGGGAGA	TCATAACTCCGGTCCCTCTG
CEBPβ	GGCCAACTTCTACTACGAGGC	CGGATCTTGTACTCGTCGCT
CEBPδ	GCCTGCGCCCTTCTACGA	CTGCTTGAAGAACTGCCGGA
FABP4	TGGGCCAGGAATTTGACGAA	GACGCATTCCACCACCAGTT
FASN	AGAGTCGGAGAACTTGCAGGA	CTGGGTTGATGCCTCCGTCC
GLUT4	ACTGGCCATTGTTATCGGCA	GTCAGGCGCTTCAGACTCTT
GAPDH	GGTGTGAACCATGAGAAGTATGACA	GGTGCAGGAGGCATTGCT
Human ChIP Primers		
Gene	**Forward Primer**	**Reverse Primer**
MEST 1	TGAAAAGGATGGGGAGGAGG	CAACAAGGGCCAGGTGAAAT
MEST 2	GTGACAGTGTGTGGGAGACA	GCGAACACAGGCATCACATA
MEST 3	GTGTGGGAAAGAGGAGGTGA	CGAGCCTTCCGTATTTCAGC
PPARγ 1	GCACCACCGATCAGAAGAGA	GCCGTCTTCCCAAGATGTTCT
PPARγ 2	TCCCTCGGTGTCAGAAACAC	GCTGCACACTTTCAGAGTTCC
PPARγ 3	AGACCAGCGGCTTTCTGAAC	TTCTTTTCCTGCCACGCTGT
SOX4 (Control)	CATGGTGCAGCAAACCAACA	TTCATGGGTCGCTTGATGTG
Pyrosequencing Primers		
Gene	**Forward Primer**	**Reverse Primer**
MEST CpGs A-D	TAAAGGGTATGAAATGGTAGGT	ATCACTTCTTTAACCTTCACTTTTATTA
MEST CpGs E-F	GGTTTTTATTTTGTTTTTAGGGAGGAT	ACCTACCATTTCATACCCTTTAC
	Sequencing Primers	
MEST CpGs A-D sequencing	ATATAAAAATACTCAAATCAAAC	
MEST CpGs E-F sequencing	GTTTTAGAGTTTAGTATGTGTTG	
Mouse mRNA Expression Primers		
Gene	**Forward Primer**	**Reverse Primer**
SOX6	TTGGGGAGTACAAGCAACTGATGC	ATCTGAGGTGATGGTGTGGTCGTT
SOX5	TCTCTGCTGACGCAAGAGAC	GTGTCCACCACATCCGCTAA
SOX9	CGAGCACTCTGGGCAATCTCA	CAATGTTGGAGATGACGTCGC
SOX13	GGACTGCGGAAGGGAACAC	GGACATCTAATCGGTCGGGC
MEST	GGCCATTGGATCCTATAAATCCGTA	GGTAGTGGCTAATGTGGTCATCCAG
ADIPOQ	TGACGACACCAAAAGGGCTC	AGAGTCCCGGAATGTTGCAG
PPARγ	CATGACCAGGGAGTTCCTCAA	AGCAAACTCAAACTTAGGCTCCAT
CEBPα	CCAAGAAGTCGGTGGACAAGA	CGGTCATTGTCACTGGTCAAC
CEBPβ	AGCGGCTGCAGAAGAAGGT	GGCAGCTGCTTGAACAAGTTC
CEBPδ	CGACTTCAGCGCCTACATTGA	CTAGCGACAGACCCCACAC
FABP4	GATGAAATCACCGCAGACG	GCCCTTTCATAAACTCTTGTGG
GLUT4	GTGACTGGAACACTGGTCCTA	CCAGCCACGTTGCATTGTAG
LDLR	CCACTTCCGCTGCAACTCA	CGTCGCAGGCCCAAAG
FASN	AGATGGAAGGCTGGGCTCTA	GAAGCGTCTCGGGATCTCTG
FABP5	CATGGCCAAGCCAGACTGTA	GGTGCAGACCGTCTCAGTTT
IMMP2L	TTGGACCGGTTTCTCTGGGA	GGAGGCATCTGGTGTGTTCA
ACACB	ACCTGCAGAACGAAGGTGAG	GACTCCTCGATCTTGAGCGG
NFAT5	GTAGTTGCTGCTGATGCTTCTT	TCTTCGGGGTTGATGGATGC
PMVK	TCGATGTGGGCTGTGTAGTG	CTCCAAGTCTGCTCTTCAGCC
ACSS2	GCATTCAGAAGGGTGACCGA	AGCAGATCTGGACATCTGGAC
DAPK1	AGCACGGGCGAGATAAACAT	TCCCACTACTCAGGTCTCGG
UBE2E2	GCCGCGAGGATCTAAGATGT	CAGCACTACAGTTGGGAGGG
MKNK2	CGTGGCGGATCCATCCTAAG	CTGGCTTTAGGTCCCTGTGG
YAF2	TGTGGTCCCTGACAGTTGTG	TGAAGAATGAGGTATCTGAGCGT
UPP2	GACTTGAAGCTGCATCATTGTGA	ATGGAAGCCATACTCTGCGG
PP1A	CATACAGGTCCTGGCATCTTGTC	AGACCACATGCTTGCCATCCAG
Mouse ChIP Primers		
Gene	**Forward Primer**	**Reverse Primer**
MEST 1	AGAATCCTTCAAGCCCATTGAT	CCCACCCTCTACTCCCGTAA
MEST 2	TCCCTAGCCATTTAGTGTGCC	AAAATTCGGGTCACCAATGCG
MEST 3	TCCCTAGCCATTTAGTGTGCC	CCTACGTGTGTTTTGAGCCC
PPARγ 1	GTGGGTGAAATTGCATGTTTGTTTT	GGAAGCCATGAGCAGAGATAAAAT

PPARγ 2	AGAATTTCTGTTCTTCTTCAGGCA	TGTTCCTGTACTCTAGAAACTTGC
SOX4 (Control)	CCCCCACTGCAGACTCTCTA	GCTGATTGGCTGTCTGAGAA

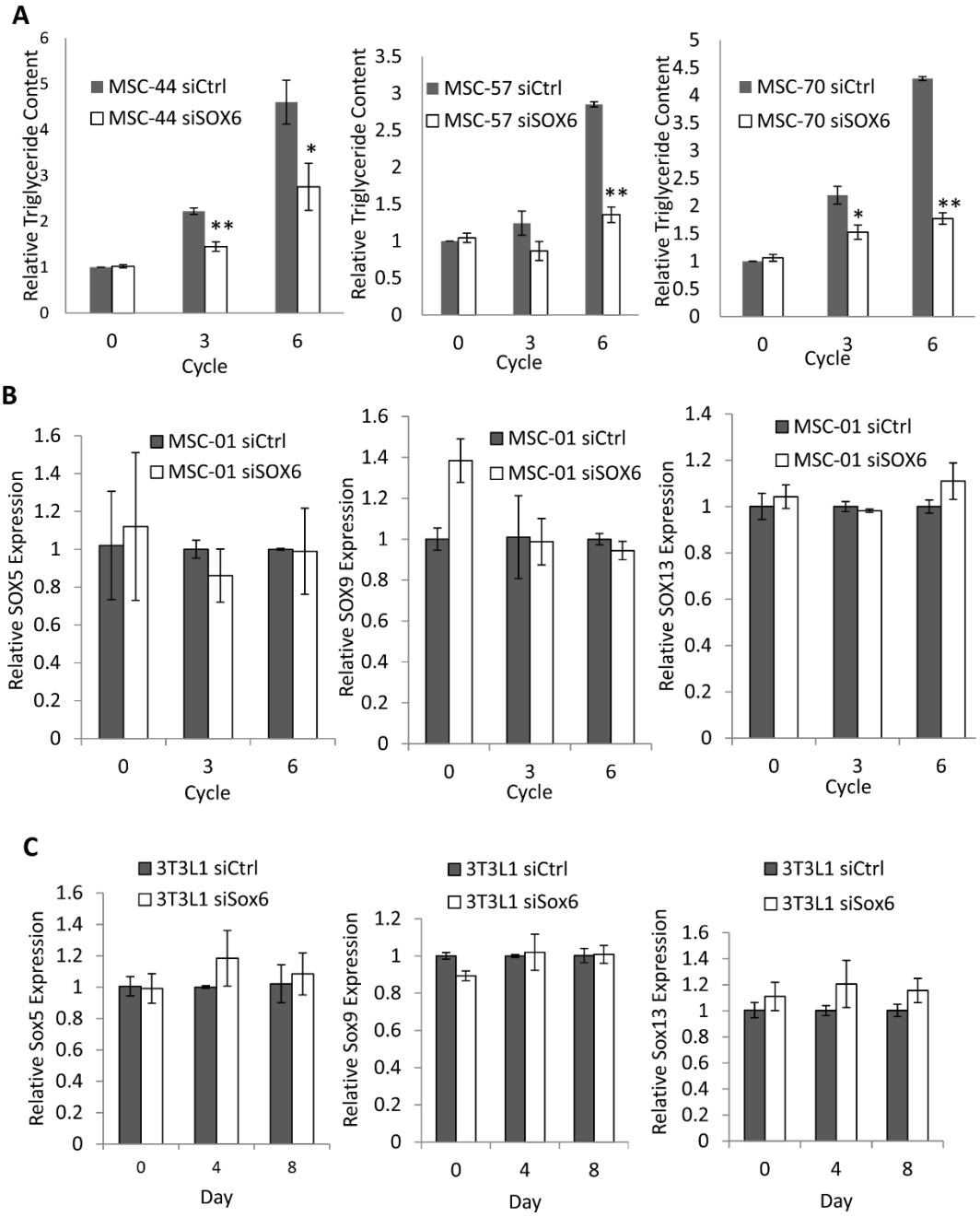
Mouse LNA Antisense Oligonucleotides

Product Name	**Sequence 5'-3-**
Negative Control	AACACGTCTATACGC
SOX6	TCTAGGTGGATTTGC



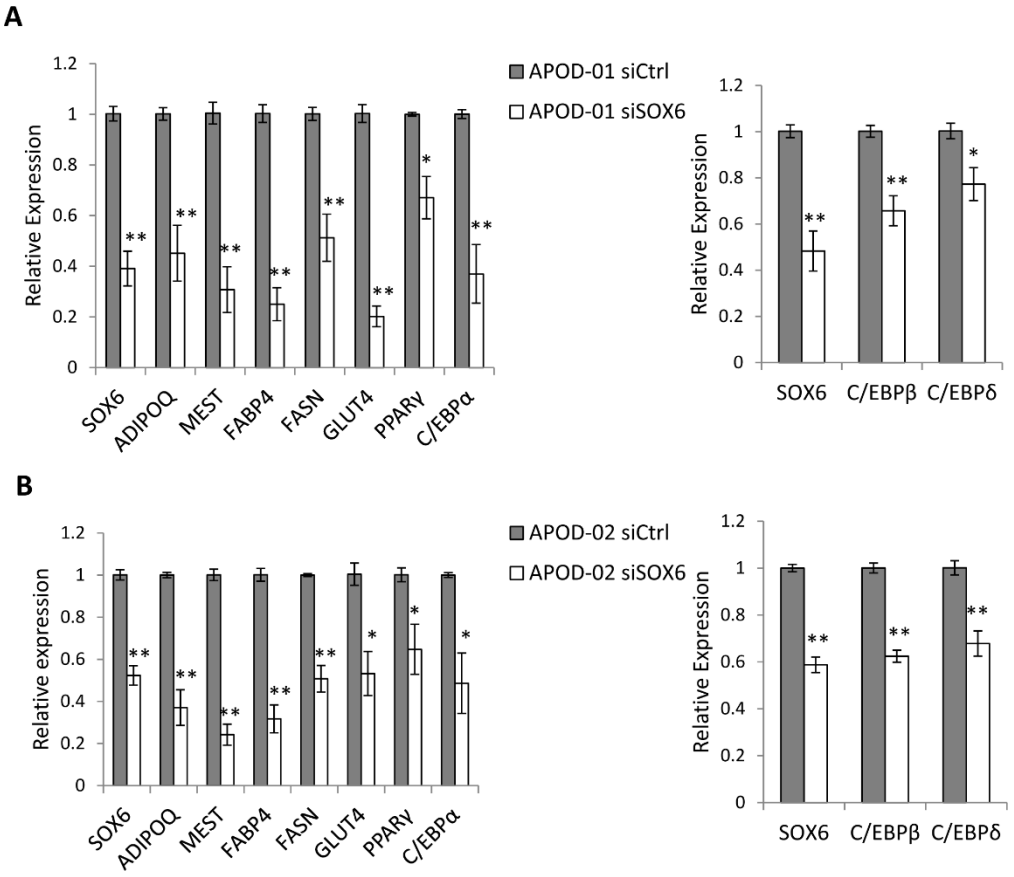
Supplementary Figure S1: SOX6 down-regulation inhibits adipocyte differentiation in both mouse and human pre-adipocytes. (A, B) Oil Red O staining (left) of siCtrl-treated or siSOX6-treated 3T3L1 and APOD-02 cells at different stages of differentiation. Images are representatives of three independent experiments. Middle panels depict the quantification of Oil Red O absorption by spectrophotometry. Data represent the mean relative absorbance ± SEM compared with siCtrl day 0

(n=3; *=p<0.05, **p<0.01). Right panels depict the amount of total triglycerides in siCtrl-treated or siSOX6-treated 3T3L1 or APOD-02 cells. Measurements were performed in triplicates and normalized against their total protein content in three separate experiments. Data are shown as mean ± SEM, relative to siCtrl day 0. A two-way ANOVA was performed to show significant difference in time points ($p < 0.0001$) and between siRNA treatment ($p < 0.0001$) over triglyceride content followed by a Student t-test (*=p<0.05, **p<0.01). (C) mRNA expression of SOX6 and adipogenic genes including FABP4, FASN, PPARγ and C/EBPα were determined by RT-qPCR in MSC-01 and MSC-44 at cycle 6 of adipocyte differentiation. Data are shown as mean fold change ± SEM relative to that of MSC-44 samples. p-values were calculated by Student t-test's analysis (*= p<0.05 and **=p< 0.01). (D) Ectopic over-expression of Sox6 in 3T3L1 (labelled as "3T3L1 Sox6 OE") increases triglyceride levels at mid stages of adipocyte differentiation. Data from 2 independent experiments are shown as mean ± SEM. A two-way ANOVA was performed to show significant difference in time points ($p < 0.0001$) and between siRNA treatment over triglyceride content followed by a Student t-test (**p<0.01).

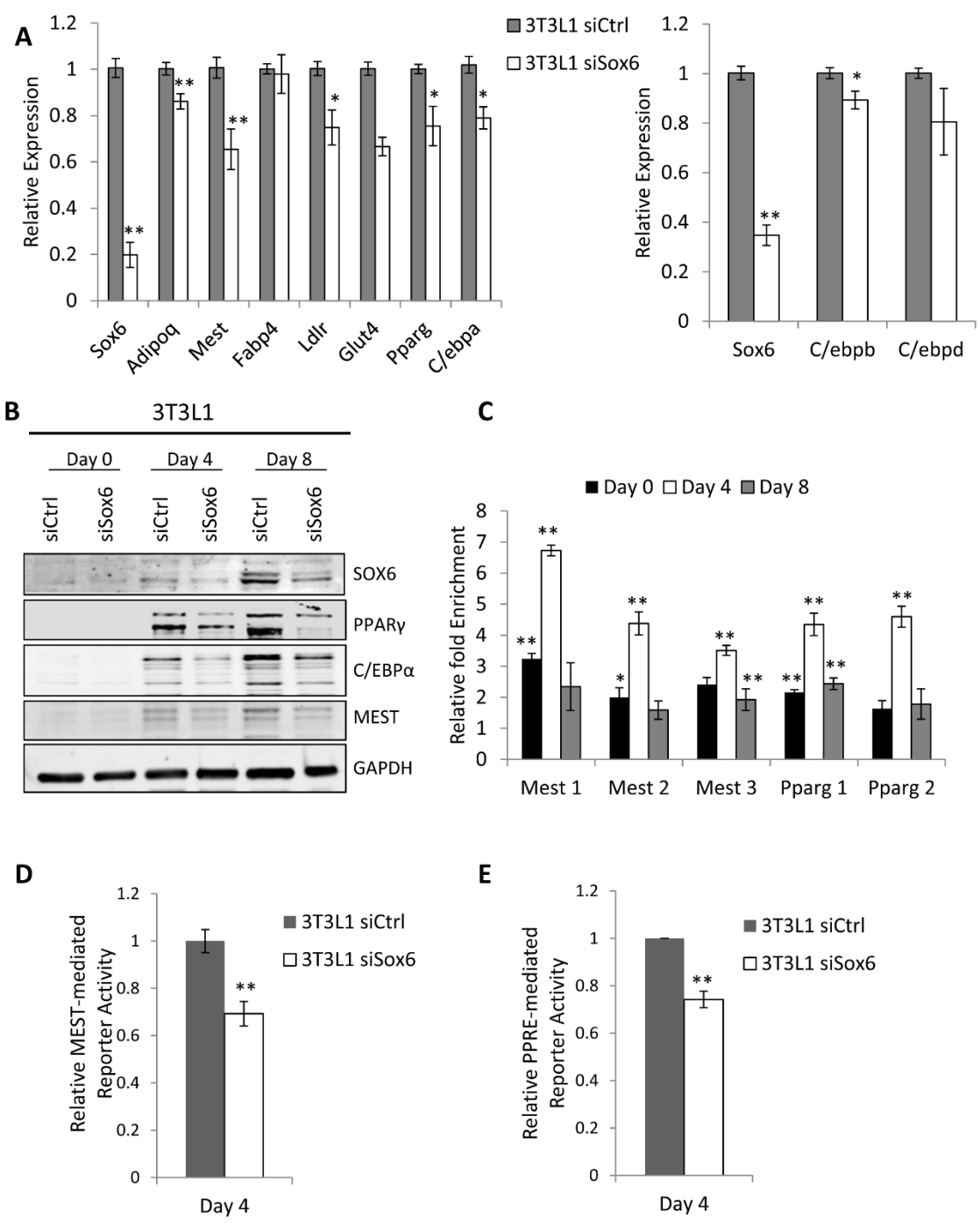


Supplementary Figure S2. SOX6 deficiency reduces total lipid accumulation in additional primary MSC lines and does not affect expression of other members of the SOX family. (A) The amount of total triglycerides in MSC-44, MSC-57 and MSC-70 after downregulation of SOX6 by siRNA treatment was measured in triplicates and normalized against the respective total protein content in three separate experiments. Data are shown as mean ± SEM, relative to siCtrl Cycle 0. A two-way ANOVA was performed to show significant difference in time points ($p < 0.0001$) points and between

siRNA treatment (p= 0.0028 for MSC-44 and p < 0.0001 for MSC-57 and MSC-70) over triglyceride content followed by a Student t-test (*=p<0.05, **p<0.01). (B, C) mRNA expression of SOX5, SOX9 and SOX13 following siSOX6 treatment in MSC-01 and 3T3L1 cells. Data are shown as mean ± SEM for SOX6 expression relative to control siRNA at each individual time point. p-values were calculated by Student t-test's analysis.

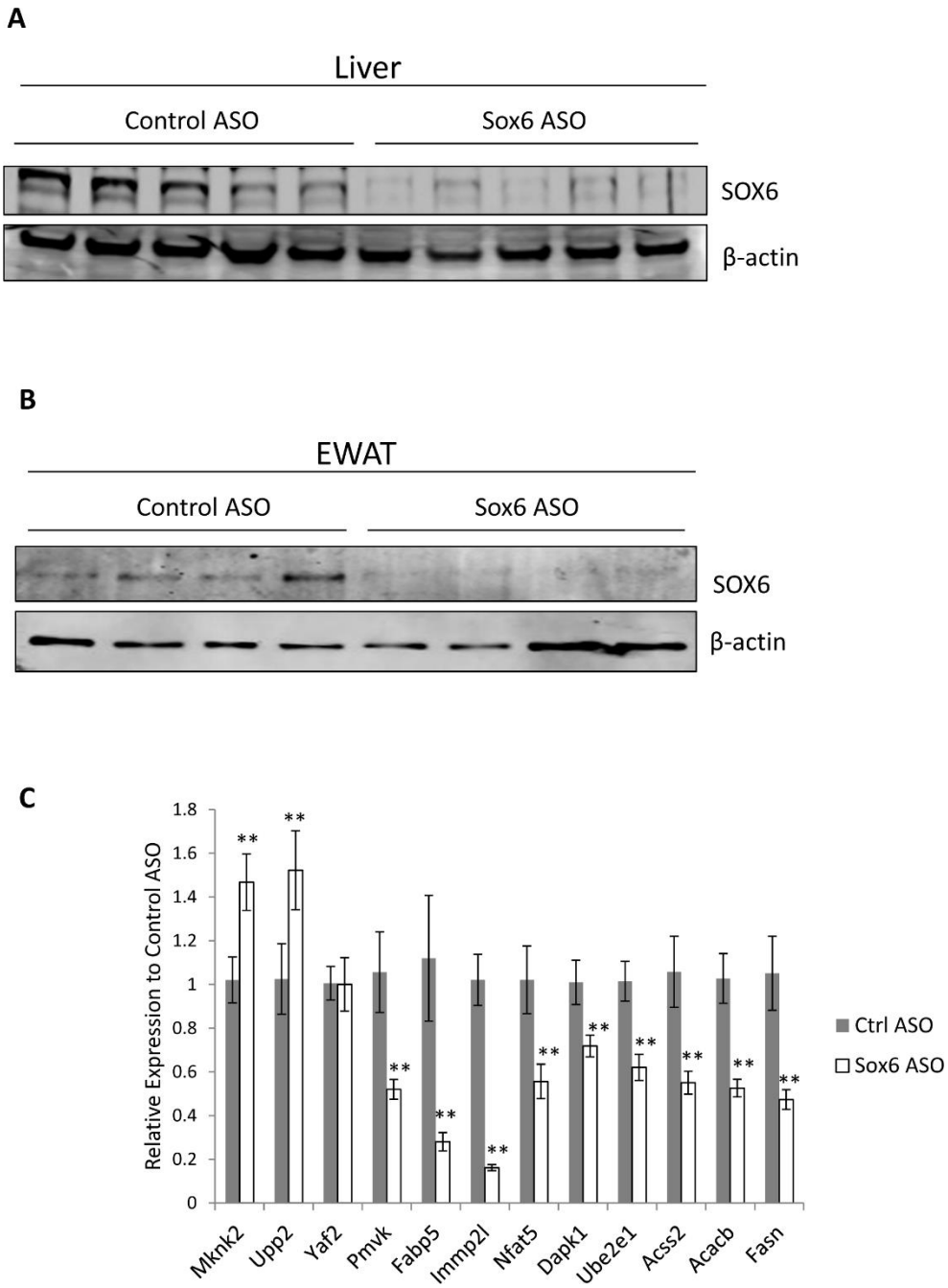


Supplementary Figure S3: SOX6 controls adipogenesis by regulating the expression of key adipogenic genes in human pre-adipocyte cells. (A, B) mRNA expression levels of adipocyte markers, ADIPOQ, MEST, FABP4, FASN, GLUT4 and two master adipogenic regulators, PPARγ and C/EBPα, were determined by qPCR in APOD-01 and APOD-02 siSOX6 treated cells in comparison with the control group (siCtrl). Data are shown as mean ± SEM of at least 3 independent experiments. p-values were calculated by Student t-test's analysis (*= $p<0.05$ and **=$p< 0.01$). Right panels show the mRNA expression levels of adipogenic initiation regulators, C/EBPβ and C/EBPδ which were determined by qPCR in siSOX6 cells in comparison with control cells (siCtrl) at day 0. Data are shown as mean ± SEM. of at least 3 independent experiments. p-values were calculated by Student t-test's analysis (*= $p<0.05$ and **=$p< 0.01$).



Supplementary Figure S4: SOX6 controls adipogenesis by binding to promoters of Mest and Pparg and by regulating the expression of key mediators of adipogenesis in mouse 3T3L1 cells. (A) mRNA expression levels of adipocyte markers, Adipoq, Mest, Fabp4, Fasn, Glut4 and two master adipogenic regulators, Pparg and C/ebpa, were determined by qPCR in siSox6 treated 3T3L1 cells in comparison with the control group (siCtrl). Data are shown as mean ± SEM of at least 3 independent experiments.

p-values were calculated by Student t-test's analysis (*= p<0.05 and **=p< 0.01). Right panels show the mRNA expression levels of adipogenic initiation regulators, C/ebpb and C/ebpd which were determined by qPCR in siSox6 cells in comparison with control cells (siCtrl) at day 0. Data are shown as mean ± SEM. of at least 3 independent experiments. p-values were calculated by Student t-test's analysis (*= p<0.05 and **=p< 0.01). (B) Protein expression of Sox6 and adipogenic markers in siCtrl- and siSox6-treated 3T3L1 cells. (C) SOX6 enrichment at the mouse Mest and Pparg promoters was measured by ChIP-qPCR at day 0, 4 and 8 of the adipocyte differentiation process in 3T3L1 cells. Data are shown as mean fold enrichment ± SEM of three independent experiments and were normalized against IgG enrichment and against a negative control site (SOX4). p-values were calculated by Student t-test's analysis (**=p< 0.01). (D and E) siRNA-mediated inhibition of Sox6 decreased luciferase expression from a Mest (D) and Pparg (E) target gene reporter construct in 3T3L1 cells at day 4 of adipocyte differentiation. Luciferase experiments were performed in triplicates on four independent occasions. Data are shown as relative mean + SEM and compared against siCtrl cells at each respective day. p-values were calculated by Student t-test's analysis (* =p<0.05, **=p<0.01).



Supplementary Figure S5: Differential gene expression in liver tissues from mice treated with Sox6 and control ASOs. Protein expression of SOX6 in the (A) liver tissues (n=5) and (B) epididymal white adipose tissues (EWAT; n=4) of control and Sox6 ASO-treated mice. (C) Differential gene expression in livers from mice treated with Sox6 ASOs (n=4) compared to the control group (n=4). mRNA expression of selected candidate genes from a gene expression microarray experiment as assessed by qRT-PCR. p-values were calculated by Student t-test's analysis (**=p< 0.01).