Supplementary Data (Terrados *et al.*)

Supplementary Dataset S1 MEF Sp2 ChIP-Seq data set obtained with Ab1 and Ab2 (FDR<0.001). (XLS)

Supplementary Dataset S2 HEK293 Sp2 ChIP-Seq data set obtained with Ab1 (FDR<0.001). (XLS)

Supplementary Dataset S3 Pathway analysis of Sp2 target genes in MEFs. (XLS)

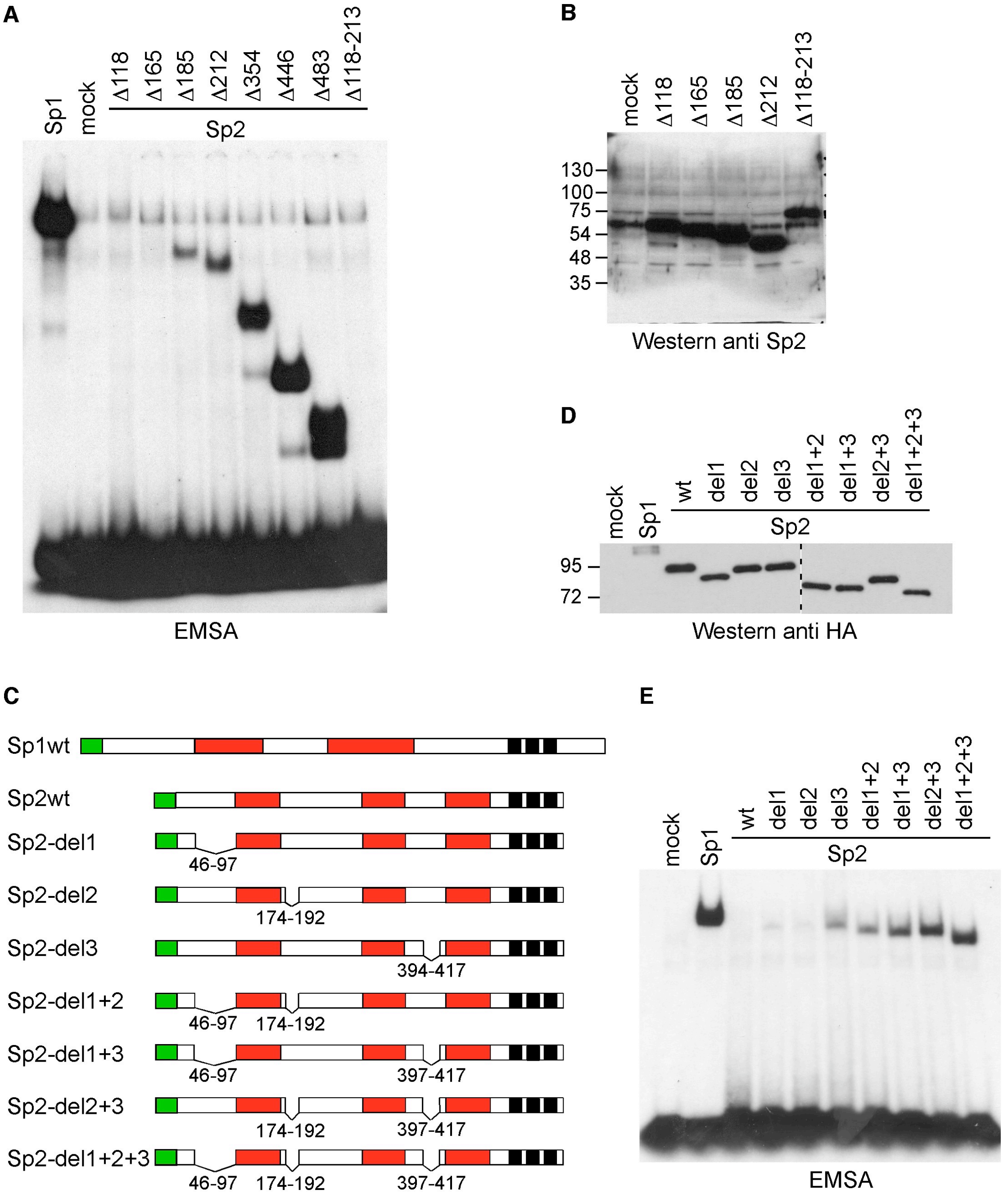
Supplementary Dataset S4 Pathway analysis of Sp2 target genes in HEK293 cells. (XLS)

Supplementary Dataset S5 List of ≥1.5 fold de-regulated genes after short-term depletion of Sp2 in MEFs. (XLS)

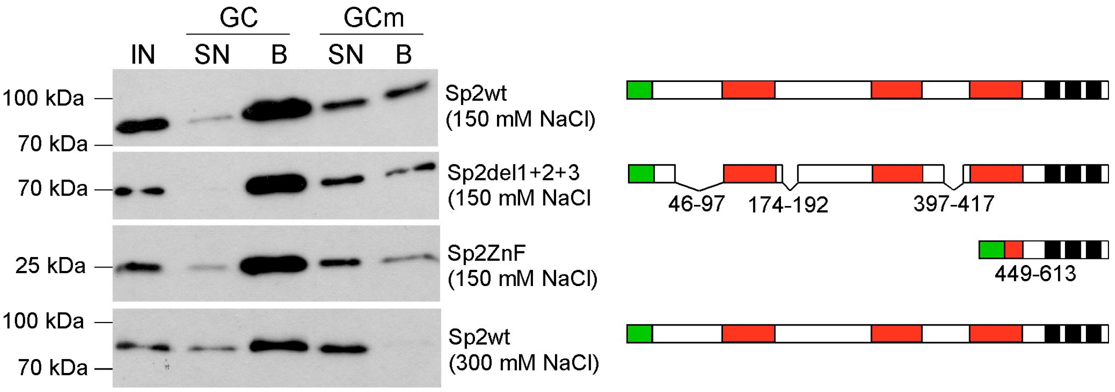
Supplementary Dataset S6 List of ≥1.5 fold de-regulated genes after long-term depletion of Sp2 in MEFs. (XLS)

Supplementary Dataset S7 Pathway analysis of direct Sp2 target genes repressed ≥1.5 fold. (XLS)

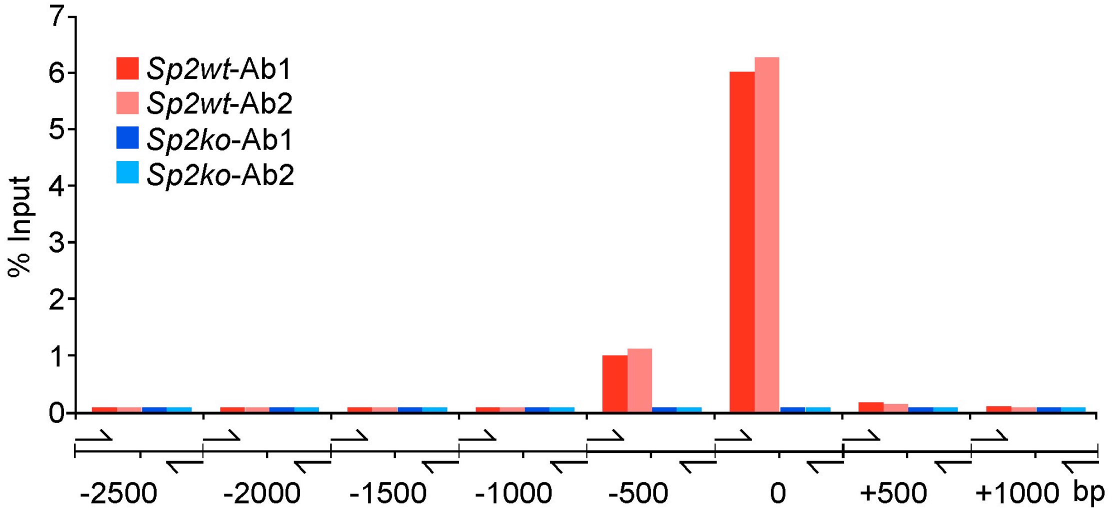
Supplementary Dataset S8 Pathway analysis of direct Sp2 target genes activated ≥1.5 fold. (XLS)



Supplementary Figure S1. Electrophoretic mobility shift analysis of Sp2 mutants. Various N-terminal and internal deletion mutants of Sp2 were transiently transfected in SL2 cells. Crude nuclear extracts were subsequently analysed by EMSA and Western blotting. Sp1-transfected cells were used as a positive and mock-transfected cells as a negative control. (**A**) EMSA with progressive N-terminal Sp2 deletion mutants. (**B**) Western blot analysis of N-terminal Sp2 deletion mutants. (**C**) Schematic drawing of internal HA-tagged Sp2 deletion mutants. The three zinc fingers of the DNA binding domain are indicated by black boxes. Glutamine-rich regions are highlighted in red and the HA epitope in green. (**D**) Western blot analysis of Sp1 and of internal Sp2 deletion mutants expressed in SL2 cells. (**E**) EMSA with nuclear extracts containing Sp2 mutant proteins with internal deletions.



Supplementary Figure S2. DNA affinity precipitation assay (DAPA) analysis of Sp2 mutants. Expression constructs for full-length Sp2 (Sp2wt), Sp2del1+2+3 and Sp2ZnF were transiently transfected in SL2 cells. Crude nuclear extracts were subsequently subjected to DAPA using a biotinylated GC box oligonucleotide (GC) and an oligonucleotide with a mutation in the Sp recognition sequence (GCm). Bound Sp2 proteins were subsequently analysed by Western blotting (anti HA). IN, input 2.5%; SN, supernatant (unbound protein) 2.5%; B, bound protein 80%. Residual binding to the GCm oligonucleotide could be prevented by high salt concentrations. A schematic drawing of HA-tagged Sp2 mutants is shown on the right side. The three zinc fingers of the DNA binding domain are indicated by black boxes. Glutamine-rich regions are highlighted in red and the HA epitope in green.



Supplementary Figure S3. ChIP-qPCR promoter walk for binding of Sp2 to its own promoter. Two different Sp2 antibodies were used for ChIP-qPCR analysis of the *Sp2* gene in wild type (*wt*) and in *Sp2ko* MEFs (*ko*). Amplification of chromosomal regions from -2500 bp to +1000 bp relative to the TSS was with eight primer pairs indicated by arrows. ChIP-qPCR values are represented as % of input.

Supplementary Table S1. Primers for ChIP-qPCR analyses.

Gene	**Primer**	**Sequence**
Cyp51	Fw	5’-TCTTGGTACAGCAGCACACC
	Rv	5’-ATGTCACCTCTGGGCTTTGT
Cyth2	Fw	5’-CTGCAACCCAAGGTTGAGAC
	Rv	5’-TGGCAGCTTTATCCTCCAAT
Hmgcr	Fw	5’-ACCCTGCAGGTCAAACTCTG
	Rv	5’-CGAACGGTCTCCCTAACAAC
Hmgcs1	Fw	5’-AGGGAAAACCCTAGCGAGTC
	Rv	5’-AAGAACGAGCAAAGCAAGGA
Hsd17b7	Fw	5’-CTCGGCCTATCTCACCTCAC
	Rv	5’-CCCTGCACCGAAGTAGAACT
Mvd	Fw	5’-GGCTATCCAGTGGTGCTTGT
	Rv	5’-AGCCTATGGACAGGATCGAA
Mvk	Fw	5’-CCTCTCAATCGCTGTTTCCT
	Rv	5’-CTTCCTGAGGCCAATCAGAG
Nfatc2ip	Fw	5’-ACCAACCAGGAAAATGGATT
	Rv	5’-CACACTGCTTCCACAAACA
Pmvk	Fw	5’-TATGTTTGGCCGGTTGTGTA
	Rv	5’-GAAAGAGCCTTGCAGCCTAGT
Sp2 (TSS)	Fw	5’-CCAGACCAACGTCACTCTAG
	Rv	5’-TACGACATCTTCCTCCCTGG
Sp2 (+500bp)	Fw	5’-TGGTCTGAACTGCAGCCTGCT
	Rv	5’-TAGGTCATCTGTTACGAGCG
Sp2 (+1000bp)	Fw	5’-TAGAGGCCTGTCAACGAGGA
	Rv	5’-TGTGCCAGTTCACTGTGAGC
Sp2 (-500bp)	Fw	5’-AATTCCCTCTAGGAAGTGCC
	Rv	5’-GCCAATCAGAAGTGCTACTG
Sp2 (-1000bp)	Fw	5’-GTGAGTGCTCTGGCTTCAAC
	Rv	5’-TGCTTGGTCTCTGCTTCATC
Sp2 (-1500bp)	Fw	5’-CAAAGTCAGAGATCTGCCAG
	Rv	5’-GTCCCCAACACTAAGCATGA
Sp2 (-2000bp)	Fw	5’-GTTGCTGTGTCTCACAAAGC
	Rv	5’-TCAGATGCTATCAGTTCTGG
Sp2 (-2500bp)	Fw	5’-CTATTGGTACCAGTTGGGTC
	Rv	5’-CTATCCTGCTGGGTGGAAAC
Srebf-2	Fw	5’-GGTGCGTTAACCCTTCTATTT
	Rv	5’-CCCCCAAGTTTGTTGTCAAT
Stat1	Fw	5’-TTGTAAACACAACCCCCTGTC
	Rv	5’-GCTGAAAACCGAAAGTACCG
Tbp	Fw	5’-CCAACTGTTTCCGCTACACA
	Rv	5’-CACATCTGATGCCGTCACTT
Tcerg1	Fw	5’-GGGTGAGTTGATTTAGACAGC
	Rv	5’-ACTAATAGCGCAAGCCGAGA

Supplementary Table S2. Primers for RT-qPCR analyses.

Gene	**Primer**	**Sequence**
Cyp51	Fw	5’-CAGGGTACACCATTCCTCCA
	Rv	5’-TCTCCAACACAACGATGACG
Ebp	Fw	5’-AGCTTCGTCGTCTGTATGGA
	Rv	5’-GCTGGAGTCCTTCGTGTAGC
Etv5	Fw	5’-CGTTGGGGTATCCAGAAGAA
	Rv	5’-CATTCGGATTCTGCCTTCAG
Fdft1	Fw	5’-ACACTGGCTGCCTGTTACAA
	Rv	5’-ATGACCTGCTTGGTTTTGCT
Foxo1	Fw	5’-GCTTGGACTGTGACATGGAG
	Rv	5’-ACTGCTCCTCAGTTCCTGCT
Foxo3	Fw	5’-GGGGAACTTCACTGGTGCTA
	Rv	5’-GGGCTGCTAACAGTCTCTGC
Gabpa	Fw	5’-TGGGGACAACGTAAGAACAAG
	Rv	5’-CCAGACGGTTCAGTTCTGCT
Gapdh	Fw	5’-GAGGCGGGTCCAAAGAGAG
	Rv	5’-AGAAGATGCGGCCGTCTCTG
Hdac6	Fw	5’-CTGGTCCTCAGCTGTGTTGA
	Rv	5’-ACGGACTGCGGTGAACTAAG
Hmgcr	Fw	5’-TGGGGCTCGTGCATAGTAAC
	Rv	5’-CAAGGAGCATGCAAAGACAA
Hmgcs1	Fw	5’-GGATCCTCAAGCTGCCTTC
	Rv	5’-TCCCAAGACATCCATTCCTC
Hsd17b7	Fw	5’-CACCAAAAACCGGAGTCTCT
	Rv	5’-AGGAACGCCTACATCAGCTC
Jun	Fw	5’-TCCCCTATCGACATGGAGTC
	Rv	5’-GCTTAAGCTGTGCCACCTGT
Kdm3a	Fw	5’-TGGGGATGTGGTGTTTATCC
	Rv	5’-TGCATCTTTCACTGCATGGT
Kdm4b	Fw	5’-GTTTGAGGATGGGTCTCAGC
	Rv	5’-ACAGGAGTGGGCAGGATCTA
Mad2l2	Fw	5’-CTCCTGTCTCATGTGGAGCA
	Rv	5’-TGGACATCCTGTTCATCTGC
Mvk	Fw	5’-CAGCACCATCTGAATGCTCT
	Rv	5’-CTGGTCTCCCAGCAGTCAA
Mvd	Fw	5’-GGTGGCACCTGTTCTTCTCT
	Rv	5’-CTTTCTCCAAATGGCACTGG
Nlk	Fw	5’-AGTTAAGGCGCACCATCATC
	Rv	5’-CATCTTCAATTCCCGGAAGA
Pmvk	Fw	5’-CTCGGAGCAGAGTCGACAG
	Rv	5’-CCCCTCAAGCCTCATCACTA
Stat1	Fw	5’-TTTCCCCATGGAAATCAGAC
	Rv	5’-CTGGAGATTACGCTTGCTTT
Srebf-2	Fw	5’-CATCCAGCAGCCTTTGATATAC
	Rv	5’-AATGATCTGAGGTTGCACCA
Taf13	Fw	5’-GTCCGTGGACATTCTCGAAG
	Rv	5’-GCTTTTCTAGCCCGTTTCAA

Tbp	Fw	5’-TCAAACCCAGAATTGTTCTCC
	Rv	5’-TGGTCTTCCTGAATCCCTTT

Supplementary Table S3. List of gene abbreviations.

Gene	**Description**	**Gene ID**
Aacs	Acetoacetyl-CoA Synthetase	78894
Acat2	Acetyl-CoA Acetyltransferase 2	110460
Acly	ATP-Citrate Lyase	104112
Acss2	Acyl-CoA Synthetase 2	60525
Baz1b	Bromodomain adjacent to zinc finger domain, 1B	22385
Brd8	Bromodomain containing 8	78656
Crem	cAMP responsive element modulator	12916
Cyp51	Lanosterol 14α-Demethylase	13121
Cyth2	Cythohesin 2	19158
Dhcr24	Desmosterol Reductase	74754
Dhcr7	7-Dehydrocholesterol Reductase	13360
Ebp	3ß-Hydroxystaroid-Δ^8,Δ^7-Isomerase	13595
Elk4	ETS domain-containing protein	13714
Etv5	Ets variant gene 5	104156
Fdps	Farnesyl Diphosphate Synthase	110196
Fdfts	Squalene Synthase	14137
Foxo1	Forkhead box O1	56458
Foxo3	Forkhead box 3	56484
Gapdh	Glyceraldehyde-3-phosphate dehydrogenase	14433
Gabpa	GA binding protein transcription factor, alpha subunit 60kDa	14390
Hdac6	Histone deacetylase 6	15185
Hltf	Helicase-like transcription factor	20585
Hmgcs1	3-hydroxy-3-methylglutaryl-CoA Synthase	208715
Hmgcr	3-hydroxy-3-methylglutaryl-CoA reductase	15357

Hsd17b7	17-ß-hydroxysteroid Dehydrogenase 7	15490
Idi1	Isopentenyl Diphosphate-Δ-Isomerase	319554
Irx2	Iroquois related homeobox 2	16372
Jun	Proto-oncogene c-Jun	16476
Kdm3a	Lys-specific demethylase 3a	104263
Kdm4b	Lys-specific demethylase 4b	193793
Klf9	Kruppel-like factor 9	16601
L3mbtl2	Lethal(3)malignant brain tumor-like protein 2	214669
Lss	Lanosterol Cyclase	16987
Mad2l2	MAD2 mitotic arrest deficient-like 2	71890
Meis	myeloid ecotropic viral integration site 1 homolog	17268 17536 17537
Mllt1	Myeloid/lymphoid or mixed lineage-leukemia translocation to 1	64144
Msh2	MutS protein homolog 2	17685
Mvd	Mevalonate Pyrophosphate Decarboxylase	192156
Mvk	Mevalonate kinase	17855
Mxd1	MAX dimerization protein 1	17119
Ncoa2	Nuclear receptor coactivator 2	17978
Nfatc2ip	Nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 2 interacting protein	18019
Nfia	Nuclear factor 1 A-type	18027
NfY	Nuclear transcription factor Y	18044 18045 18046
Nlk	Nemo like Kinase	18099
Nsdhl	NAD(P)H Steroid Dehydrogenase like	18194
Pax9	Paired box gene 9	18511
Pbx	pre-B-cell leukemia homeobox	18514 18515 18516 80720
Pmvk	Phosphomevalonate kinase	10654
Rsf1	Remodeling and spacing factor 1	233532

Sc4mol	Sterol C4-Methyl Oxidase	66234
Sc5d	Sterol C5-Desaturase	235293
Sp1	Specificity protein 1 transcription factor	20683
Sp2	Specificity protein 2 transcription factor	78912
Sp3	Specificity protein 3 transcription factor	20687
Sp4	Specificity protein 4 transcription factor	20688
Sqle	Squalene Epoxidase	20775
Stat1	Signal transducer and activator of transcription 1	20846
Stat2	Signal transducer and activator of transcription 2	20847
Taf13	TATA box binding protein (TBP)-associated factor, 18kDa	99730
Tbp	TATA box binding protein	21374
Tbx3	T-box protein 3	21386
Tcerg1	Transcription elongation regulator 1	56070
Tle1	Transducin-like enhancer of split 1	21885
Tm7sf2	Sterol C14-Reductase	73166
Trp53bp1	Transformation related protein 53 binding protein 1	27223
Ung	Uracil DNA glycosylase	22256