

Supplementary Data

Title:

LSD1 mediates metabolic reprogramming by glucocorticoids during myogenic differentiation

Authors:

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SUPPLEMENTARY FIGURE LEGENDS

Supplementary Figure S1. LSD1 inhibition that does not interfere with myogenic differentiation. **(A)** Experimental procedures used: C2C12 mouse myoblasts were differentiated to myotubes in the absence or presence of LSD1 inhibition and then subjected to the indicated analyses. **(B)** Expression levels of differentiation marker genes in day 7-C2C12 cells treated with LSD1 inhibitors (n = 4). Quantitative RT-PCR data were normalized to values for the *36B4* gene, shown as fold differences against vehicle-treated controls. Concentrations of TC and S2101 were 10^{-4} and 10^{-5} M, respectively. **(C)** Myogenic differentiation of C2C12 cells under LSD1 inhibition. Cells were prepared as described for **(A)**. Myotube formation was analyzed by immunofluorescence imaging of myosin heavy chain (MHC). Scale bar, 100 μ m. **(D)** Quantitative analyses of myotube formation under S2101 treatment. The number of nuclei, ratio of MHC-expressing nuclei to total nuclei, and area and intensity of the MHC signal are shown for control and S2101-treated cells. Values are means \pm s.d. of 3 assay wells. For each well, 30 fields were counted.

Supplementary Figure S2. Effects of LSD1 inhibition on gene expression in differentiating myoblasts. **(A)** GSEA results for genes upregulated by LSD1 inhibition. Fourteen pathways were identified with statistically significant differences (p -value < 0.05 and FDR q -value < 0.25). Pathways related to lipid metabolism are highlighted in red. **(B)** Venn diagram of the genes with expression decreased by 1.5-fold or more by treatment with LSD1 inhibitors, TC or S2101 (left). Cells were collected at 48 h after myogenic induction. Controls were treated with vehicle. GSEA results for genes downregulated by LSD1 inhibition (right). Five pathways were identified with

statistically significant differences (p -value < 0.05 and FDR q -value < 0.25).

Supplementary Figure S3. Effects of LSD1 inhibition on metabolic properties of C2C12 cells. (A and B) Effects of LSD1 inhibition on the OXPHOS capacity of differentiated C2C12 cells. OCR/ECAR: the ratio of oxygen consumption rate (OCR, **Figure 1E**) to extracellular acidification rate (ECAR) (A) and ECAR (B) are shown ($n = 10$). During real-time measurements, respiratory chain inhibitors were added to the medium at the indicated time points. Values are means \pm s.d. (C) Heatmap showing expression change of glycolysis related genes in LSD1-inhibited C2C12 cells. Expression data were extracted from microarray analyses described in **Figure 1A** and **S7**. Values are shown as fold differences against the average of each control. $*p < 0.05$, $**p < 0.01$.

Supplementary Figure S4. LSD1 enrichment relative to histone modifications and RNA polymerase II peaks on day 2 (A) or 5 (B). Data are presented in the same manner as for **Figure 2C**.

Supplementary Figure S5. Distribution of LSD1-bound sites in differentiating (day 2) or differentiated (day 5) myoblasts. Enrichment of LSD1 at the oxidative *Atgl* (A) and *Pgcl α* (B) genes, the glycolytic *Gapdh* (C) gene and the slow fiber-associated *Tnncl* (D) gene loci. (E) No enrichment of LSD1 at the fast fiber-associated *Myh4* gene locus. ChIP-seq data were visualized using Strand NGS software (Strand Genomics). Histone modifications at the *Pgcl α* (B) and *Tnncl* (D) gene loci in control cells (described in **Figure 3C**) and publicly available ChIP-seq data for Rest, Max, Six4, MyoD and

myogenin are also shown (Data IDs are listed in **MATERIALS AND METHODS**).

Supplementary Figure S6. Scatter plots show the correlation between LSD1 enrichment and changes in H3K4 methylation by LSD1 inhibition. LSD1-enriched regions in C2C12 cells (day 2) are shown. The x-axis shows the enrichment levels of LSD1 in these regions and the y-axis shows changes in H3K4me1 (**A**), H3K4me2 (**B**) and H3K4me3 (**C**) enrichment levels induced by LSD1 inhibition. Enrichment values were normalized over input and are shown as log₂ ratio. The areas with more than 2.5 log values in the x-axis and with more than 0.5 or less than -0.5 log values in the y-axis are indicated by boxes. The region numbers included in each area are shown.

Supplementary Figure S7. Effects of LSD1 knockdown in C2C12 myoblasts. (**A**) LSD1 expression in shRNA-introduced cells. Protein was collected from C2C12 cells stably expressing shRNA at 48 h after myogenic induction. (**B**) Light microscope images of LSD1-KD C2C12 cells. sh*Lsd1*- or shControl-expressing C2C12 cells were analyzed at 7 d after myogenic induction. Scale bar, 500 μ m. (**C**) Venn diagram of the genes induced by 1.2-fold or more by LSD1-KD and LSD1-bound genes with expression upregulated by LSD1 inhibitors (**Figure 3B**). Microarray analysis was performed in sh*Lsd1*-expressing C2C12 cells at 48 h after myogenic induction. (**D**) Expression levels of oxidative metabolism and myogenesis genes in LSD1-KD cells at 48 h after myogenic induction (n = 3). Values are shown as fold differences against control shRNA-expressing samples. (**E** and **F**) H3K4me1 (**E**) and H3K4me2 (**F**) enrichment at LSD1-bound regions in LSD1-KD C2C12 cells. CHIP-qPCR analyses were performed in sh*Lsd1*-expressing C2C12 cells at 48 h after myogenic induction.

Values are means \pm s.d. * p < 0.05, ** p < 0.01.

Supplementary Figure S8. Glucocorticoid treatment decreases the amount of LSD1 protein. **(A)** Procedures for sample preparation: C2C12 mouse myoblasts were differentiated to myotubes, then treated with hormones before being subjected to RNA and protein analyses. **(B)** Expression of LSD1 protein in C2C12 myotubes under various hormone treatments. Administered hormones were T: testosterone (10^{-8} M), E2: estradiol (10^{-8} M), Ins: insulin (10^{-7} M), EtOH: ethanol vehicle (0.1%), Dex: dexamethasone (10^{-6} M) and T3: triiodothyronine (10^{-8} M). Band densities were quantified by densitometry and normalized to those for histone H3. Values are shown as fold differences against those for the vehicle EtOH-treated control. **(C and D)** Expression of *LSD1* mRNA in C2C12 myotubes (C) and primary myoblasts (D) under Dex treatment (n = 3). qRT-PCR values are presented as fold differences, against those for vehicle treated controls. Values are means \pm s.d. NS: no significant difference.

Supplementary Figure S9. Glucocorticoid-induced *Jade2* expression results in LSD1 degradation. **(A)** Effect of proteasome inhibition on LSD1 protein under Dex treatment (n = 3). C2C12 cells were differentiated for 48 h and then treated with Dex (10^{-6} M) for 24 h. Cells were also treated with cycloheximide (CHX, 100 μ g/mL) and MG132 (10^{-5} M) for 6 h before harvest. **(B)** Glucocorticoid receptor (GR) occupancy the *Jade2* gene locus. ChIP analyses were performed using differentiating C2C12 cells treated with Dex for 48 h (n = 3). Numbers 1–6 indicate the sites used for qPCR experiments. Fold enrichment values were calculated relative to control IgG. **(C)** Nuclear accumulation of GR upon Dex treatment in Hepa1-6 cells. GR expression and accumulation into nuclei

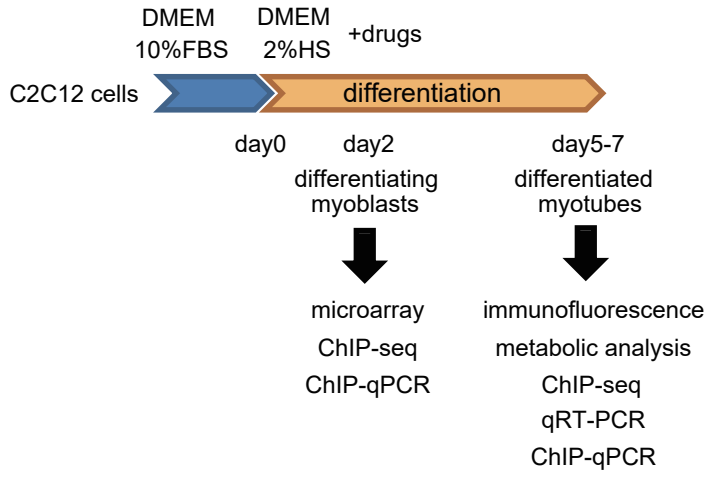
was analyzed by immunofluorescence staining, using cells treated with EtOH (control) or Dex for 24 h. Scale bar, 10 μm . **(D)** Effect of Jade2 knockdown on LSD1 protein under Dex treatment (n = 3). Hepa1-6 cells were transfected with si*Jade2*. At 24 h after transfection, cells were treated with Dex (10^{-6} M) for 48 h, together with CHX (100 $\mu\text{g}/\text{mL}$) for 6 h before harvesting samples. Target sequences of siRNA are shown in **MATERIALS AND METHODS**. **(E)** Expression of *LSD1* mRNA in gastrocnemius (Gas) and soleus (Sol) (n = 5). qRT-PCR values are presented as fold differences relative to those for Gas. **(F)** Expression of *Jade2* gene in fasted mice (n = 5). Microarray data from a public database (NCBI GSE46495) was used to calculate *Jade2* expression in mouse tissues after 24 h fasting. Values are fold differences against those for *ad libitum* fed mice, means \pm s.d. * $p < 0.05$, ** $p < 0.01$. NS: no significant difference.

Supplementary Figure S10. Treatment with Dex activates slow myosin expression. **(A)** Expression levels of myosin genes in C2C12 myotubes treated with Dex and S2101 (n = 3). Values are fold differences against vehicle-treated controls. **(B)** Expression of slow-myosin heavy chain (slow-MHC) in Dex- and S2101-treated cells. C2C12 cells on myogenic day 5 were analyzed by immunofluorescence microscopy. Scale bar, 100 μm . **(C)** Quantitative analyses of the images obtained in (B). The areas of slow-MHC signal, intensities of slow-MHC signal and the ratios of these parameters are shown. Values are means \pm s.d. of 3 assay wells. For each well, 30 fields were counted. Values are means \pm s.d. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

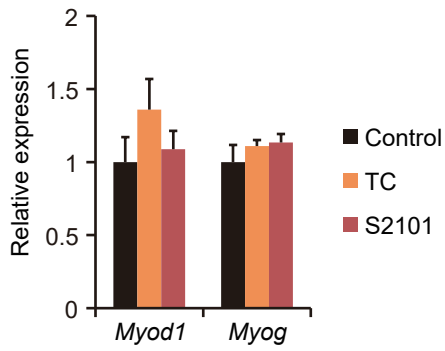
Supplementary Figure S11. Schematic model of LSD1-mediated metabolic programming in differentiating myoblasts under the action of a glucocorticoid. Glucocorticoid via the glucocorticoid receptor (GR) induces expression of JADE-2, a ubiquitin E3 ligase for LSD1, resulting in de-repression of the target genes involved in oxidative metabolism.

Supplementary Figure S12. Uncropped western blot membranes presented in this study. Areas surrounded by black boxes are those shown in individual figures.

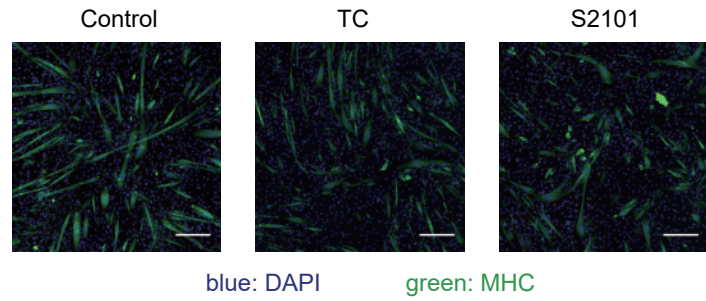
A



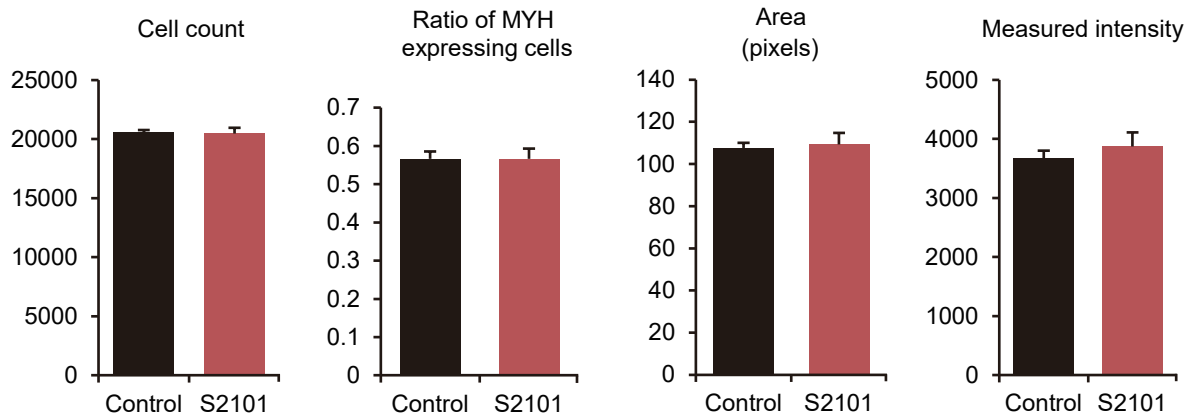
B



C



D



A

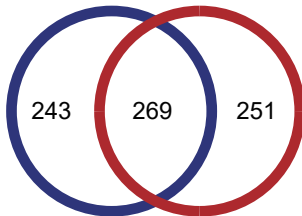
upregulated by LSD1 inhibition

NAME	NOM p-value	FDR q-value
KEGG_STEROID_BIOSYNTHESIS	<0.001	0.007131594
KEGG_LYSOSOME	<0.001	0.007186448
KEGG_GLUTATHIONE_METABOLISM	<0.001	0.008344005
KEGG_SPHINGOLIPID_METABOLISM	0.002631579	0.01331426
KEGG_DRUG_METABOLISM_CYTOCHROME_P450	0.002604167	0.013592466
KEGG_BIOSYNTHESIS_OF_UNSATURATED_FATTY_ACIDS	0.014117647	0.1463684
KEGG_METABOLISM_OF_XENOBIOTICS_BY_CYTOCHROME_P450	0.02676399	0.15217118
KEGG_EPITHELIAL_CELL_SIGNALING_IN_HELICOBACTER_PYLORI_INFECTION	0.005347594	0.15309496
KEGG_FATTY_ACID_METABOLISM	0.011235955	0.1558389
KEGG_INTESTINAL_IMMUNE_NETWORK_FOR_IGA_PRODUCTION	0.03141361	0.16073199
KEGG_ABC_TRANSPORTERS	0.01038961	0.16581017
KEGG_OXIDATIVE_PHOSPHORYLATION	0.003333333	0.178059
KEGG_PROPYANOATE_METABOLISM	0.046035804	0.22476496
KEGG_PEROXISOME	0.026865672	0.2373898

B

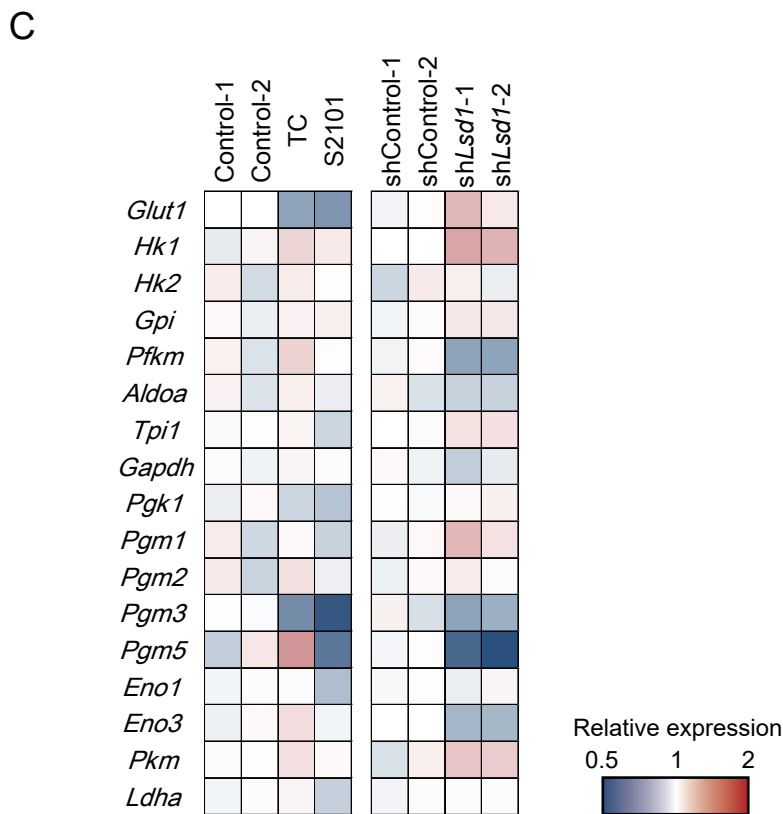
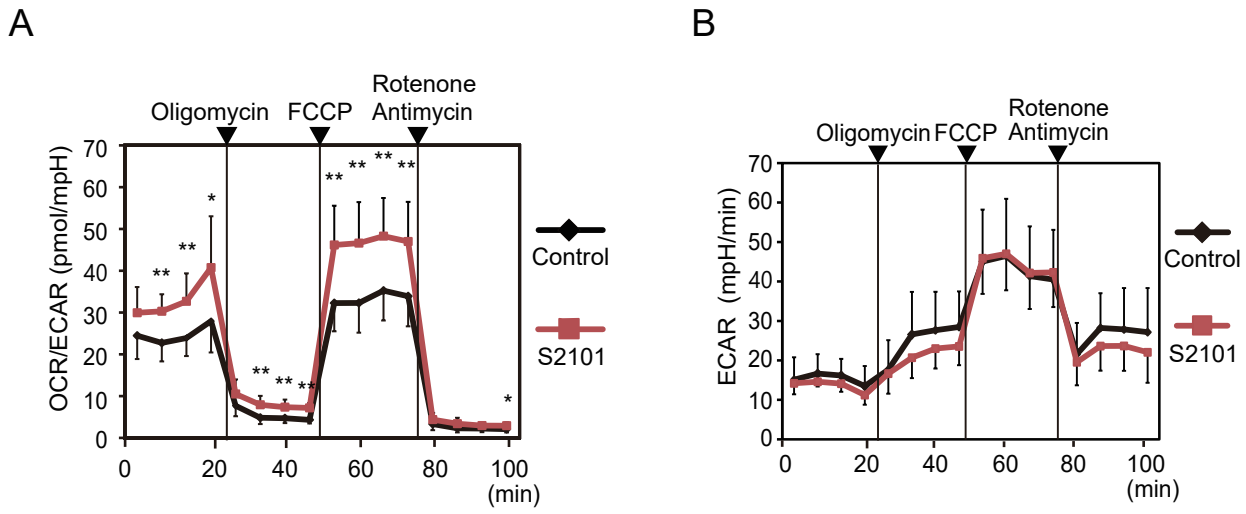
decreased <1.5 fold decreased <1.5 fold

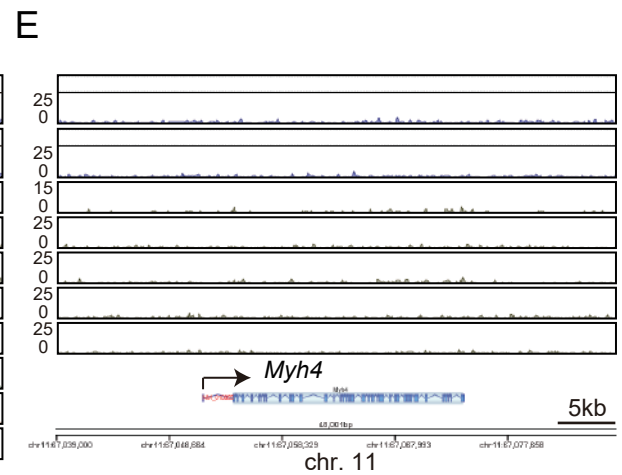
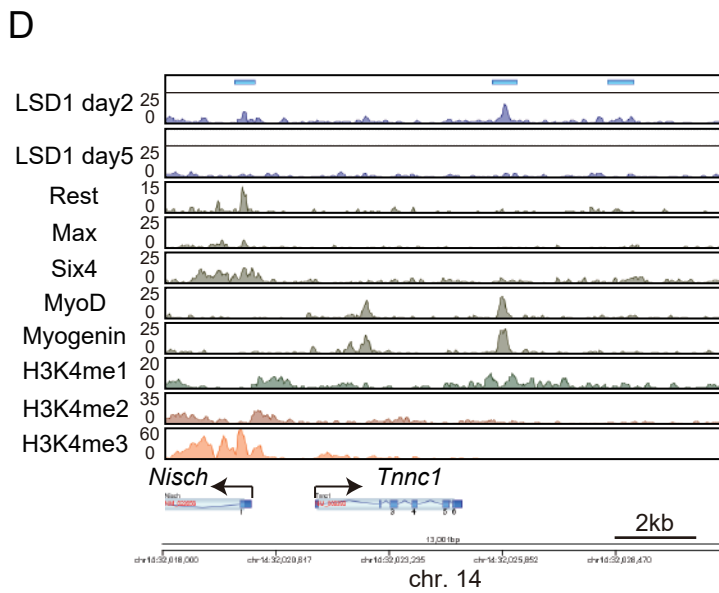
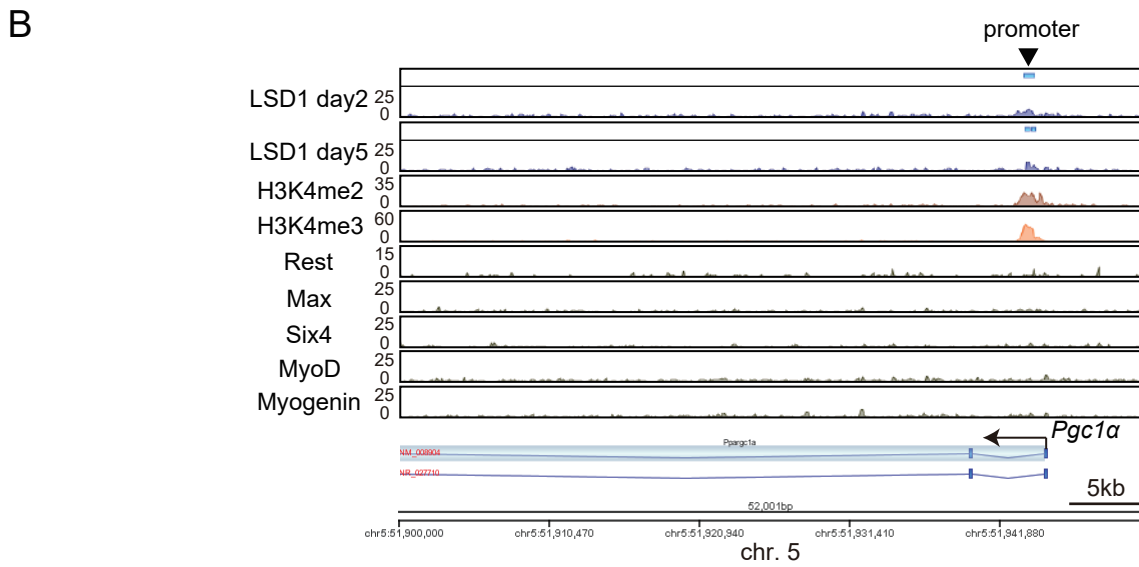
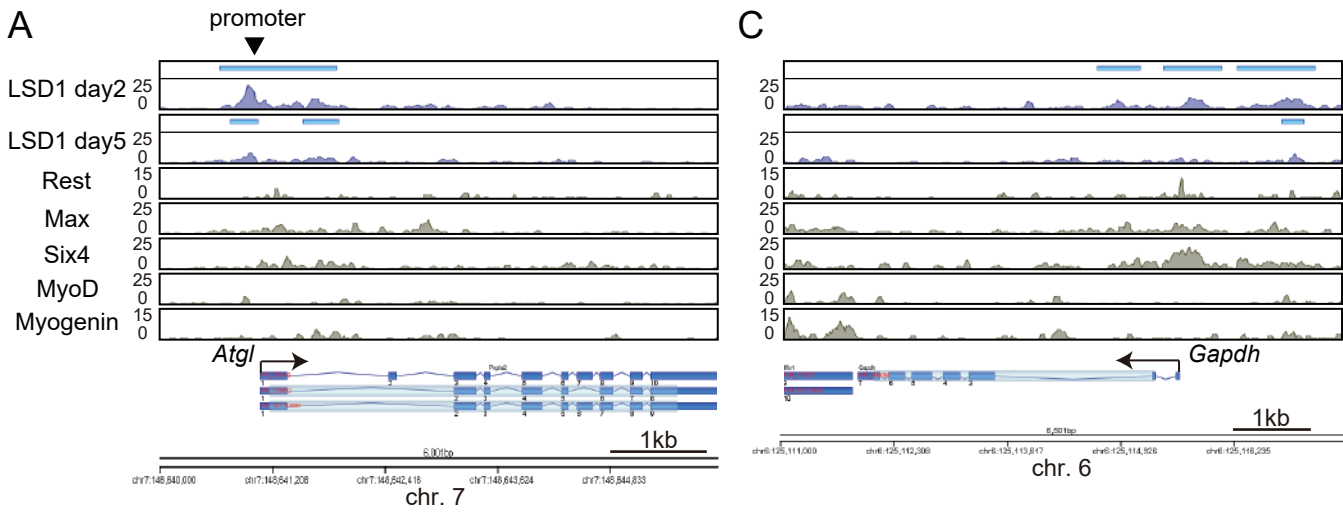
by TC by S2101
(512 genes) (520 genes)

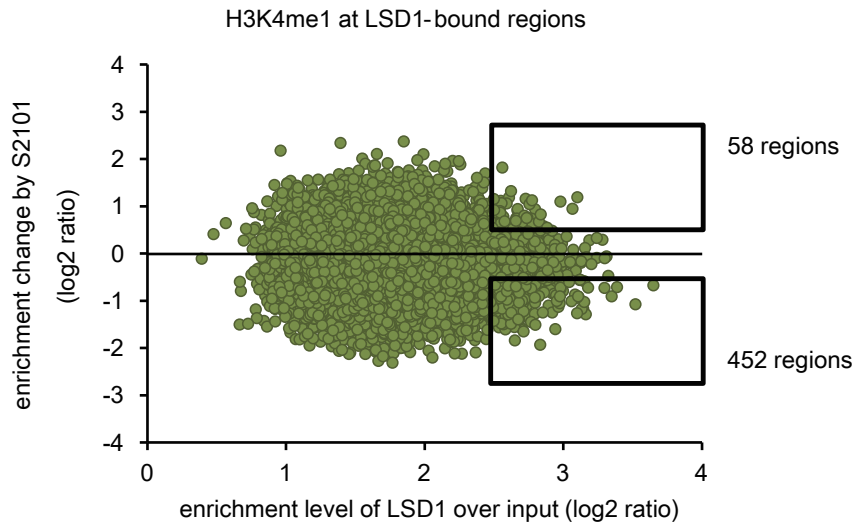
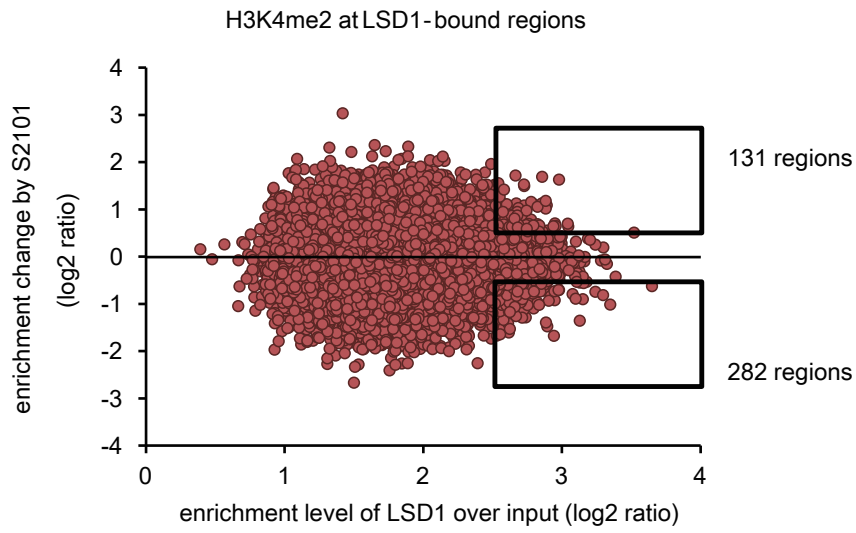
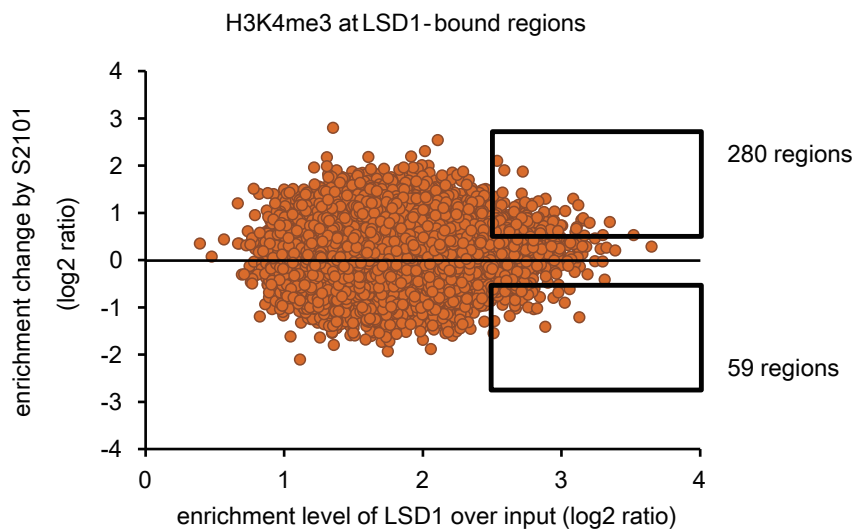


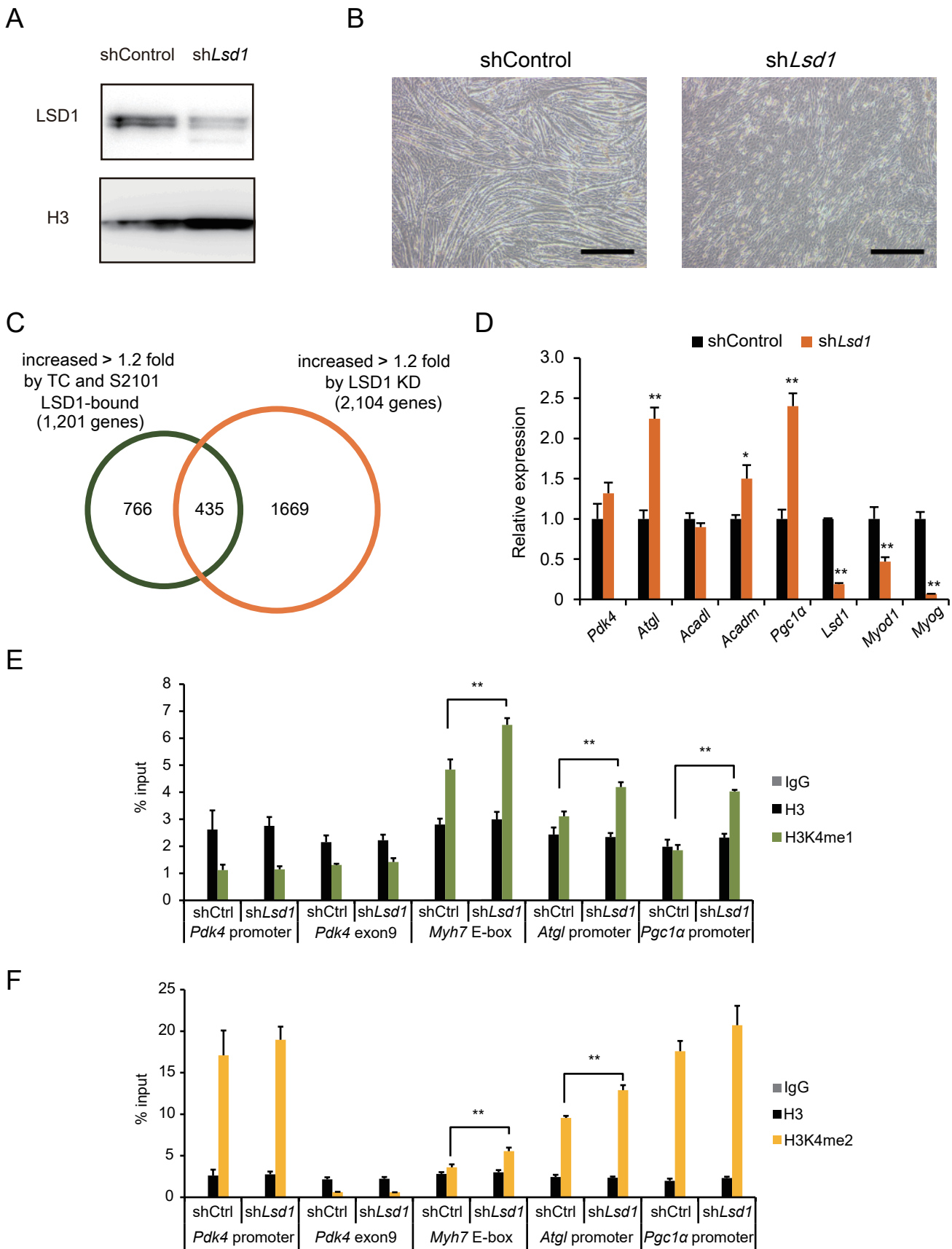
downregulated by LSD1 inhibition

NAME	NOM p-value	FDR q-value
KEGG_CELL_CYCLE	<0.001	0.004345598
KEGG_DNA_REPLICATION	0.001618123	0.021393025
KEGG_MISMATCH_REPAIR	0.026086956	0.23018923
KEGG_FOCAL_ADHESION	0.007032349	0.2200881
KEGG_ECM_RECEPTOR_INTERACTION	0.015360983	0.21840344

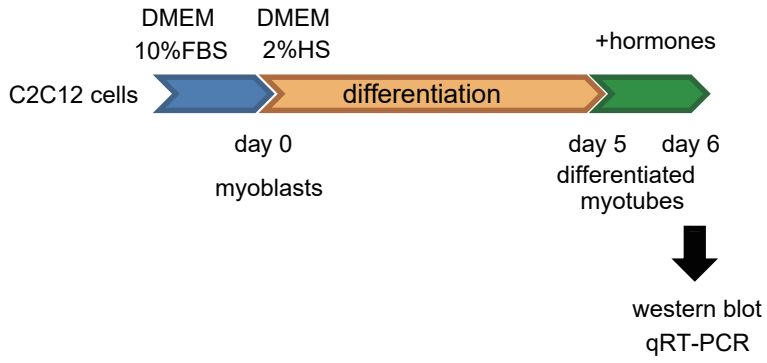




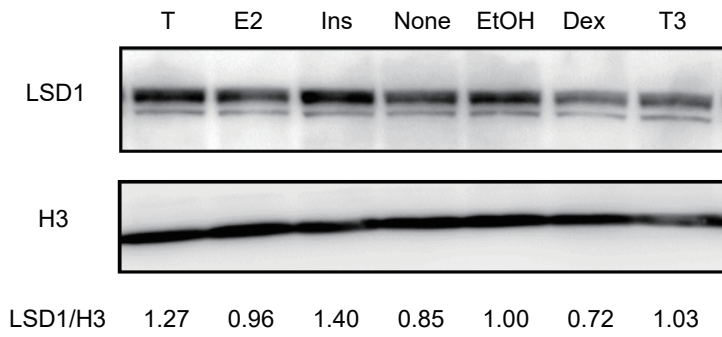
A**B****C**



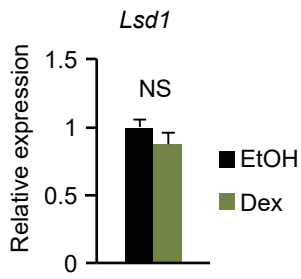
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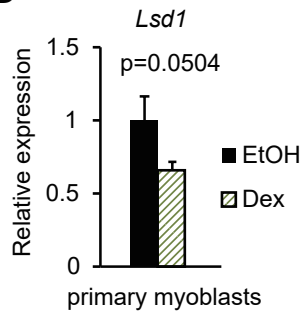
B

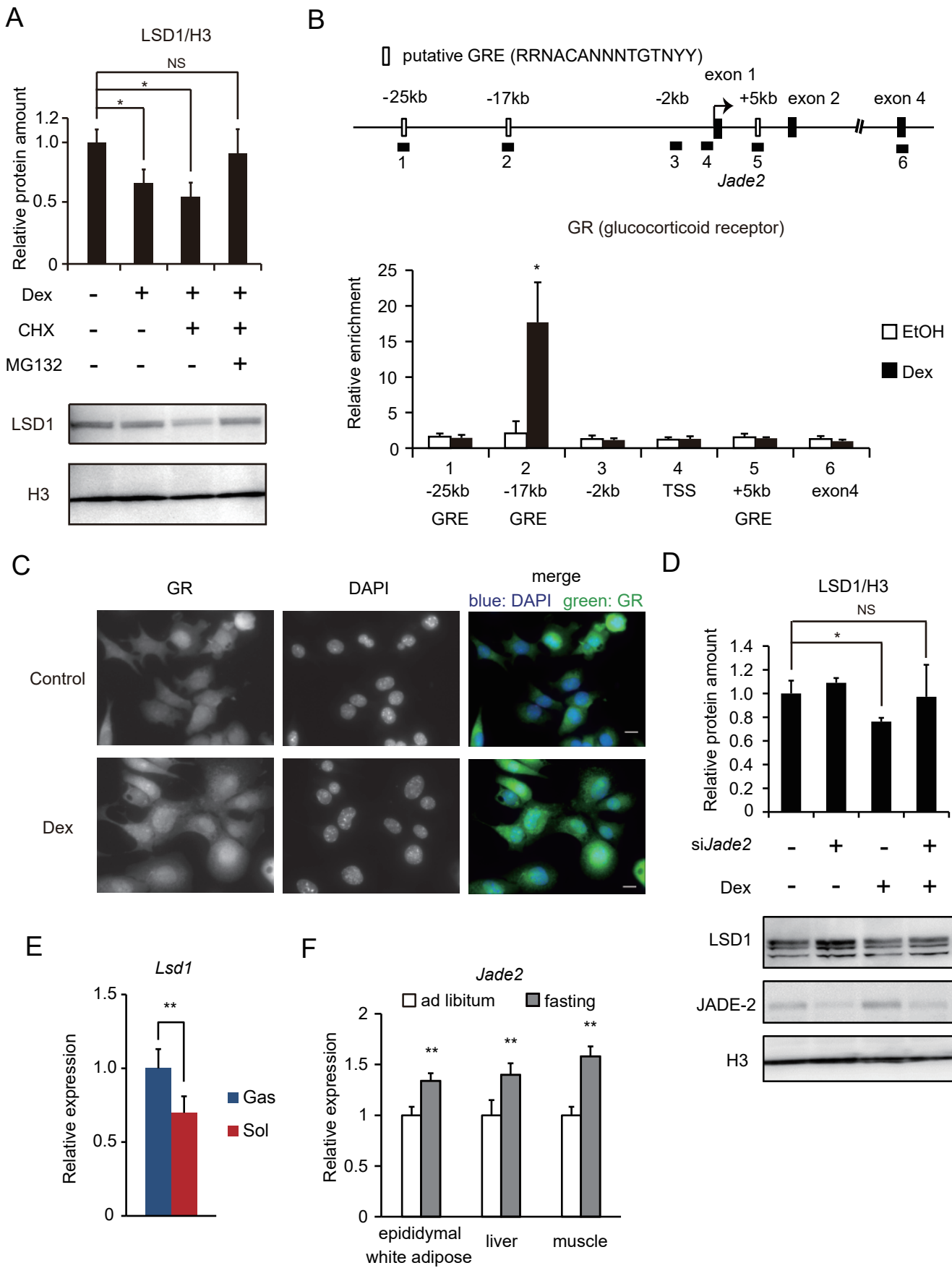


C

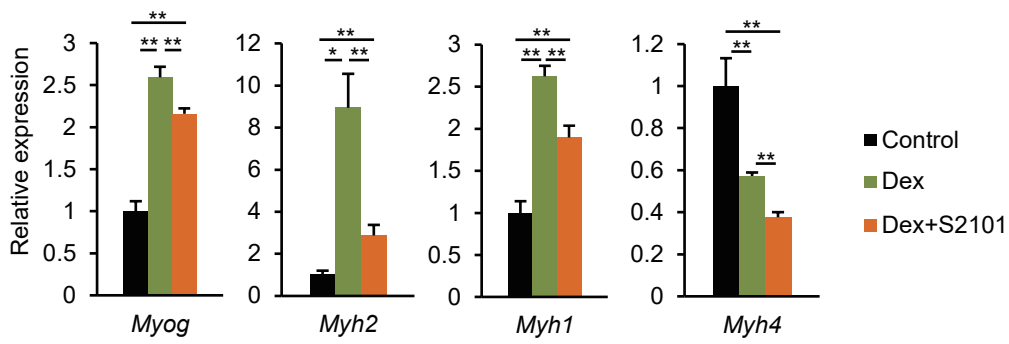


D

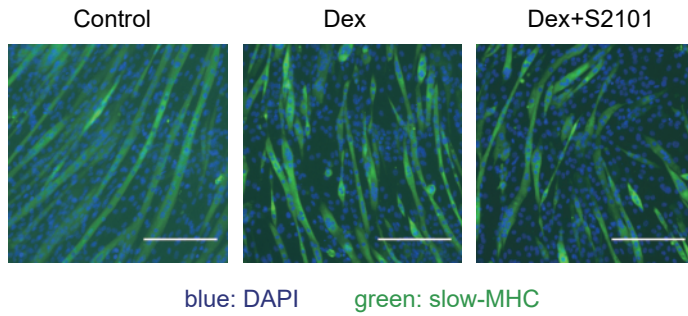




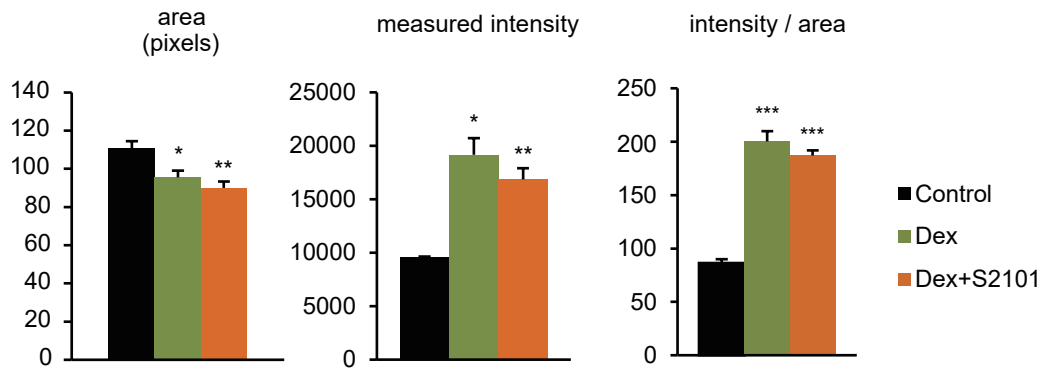
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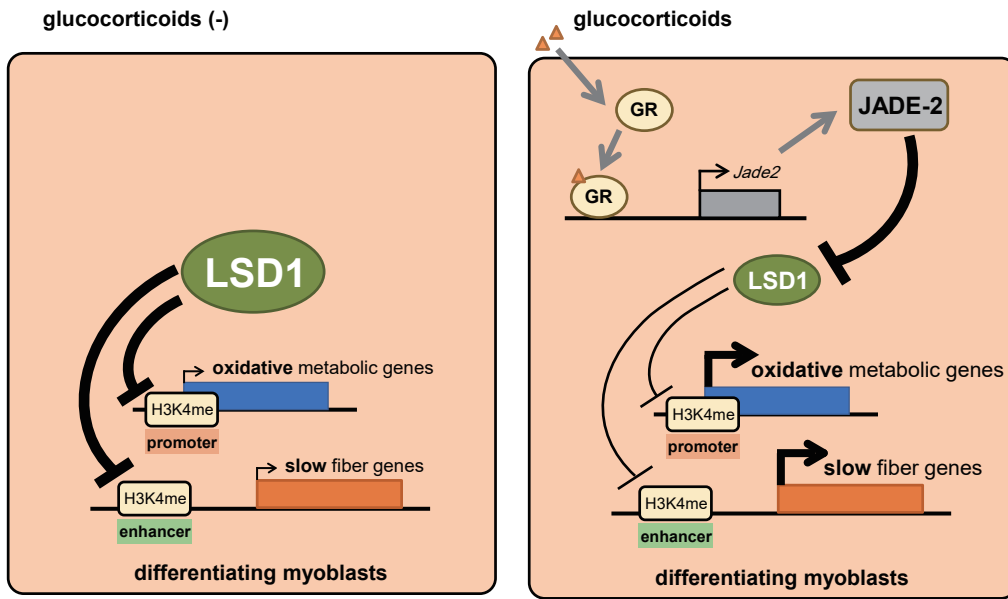


B



C





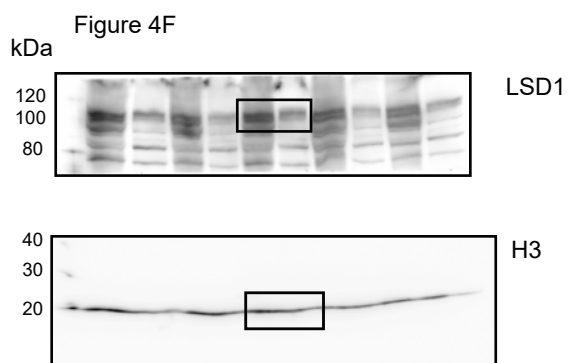
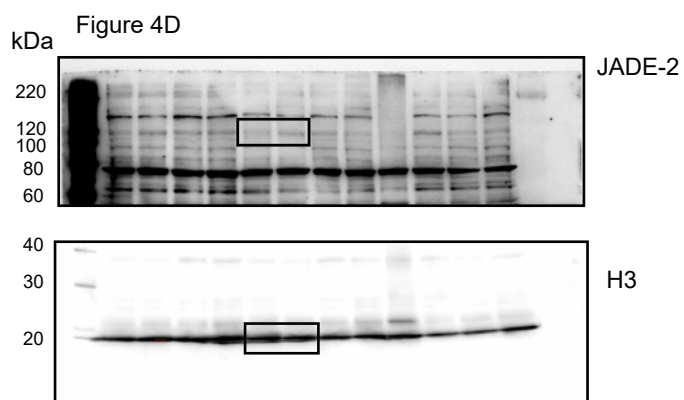
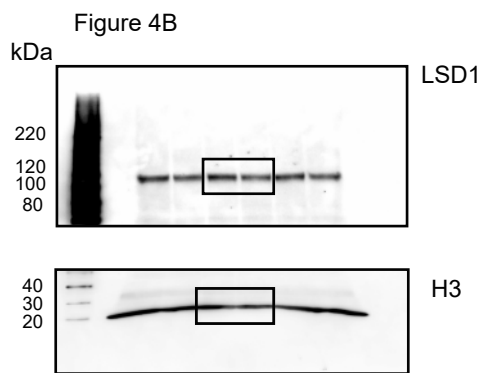
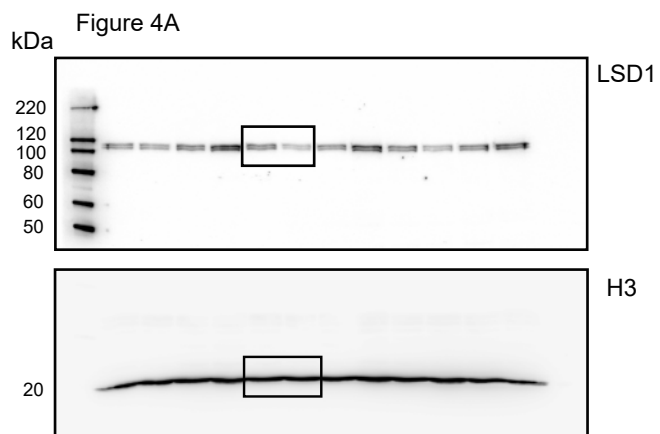


Figure 4G

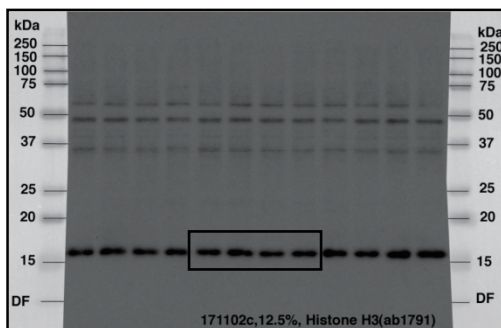
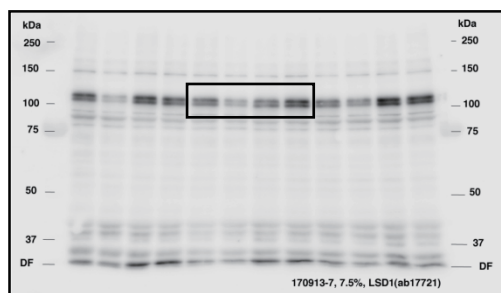


Figure 4I

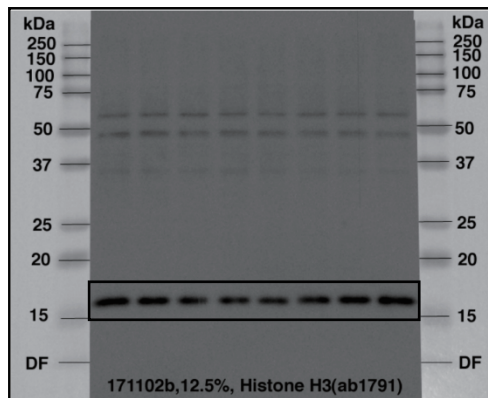
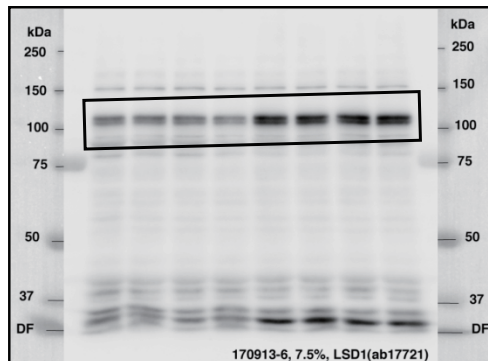


Figure S7A

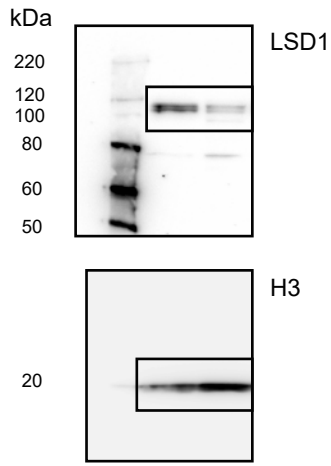


Figure S8B

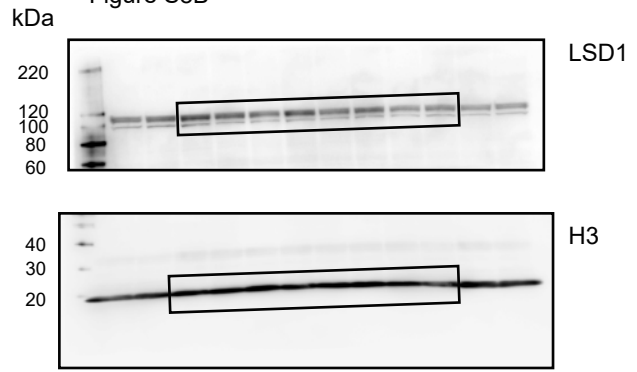


Figure S9A

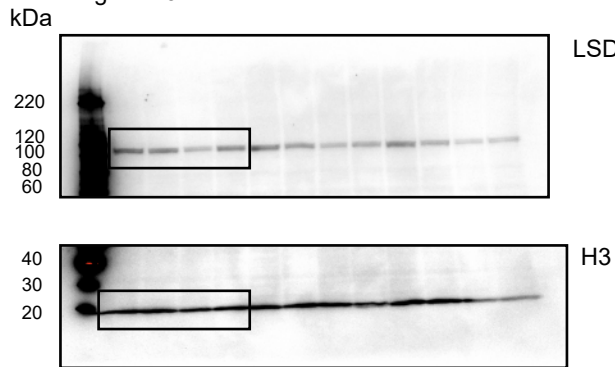


Figure S9D

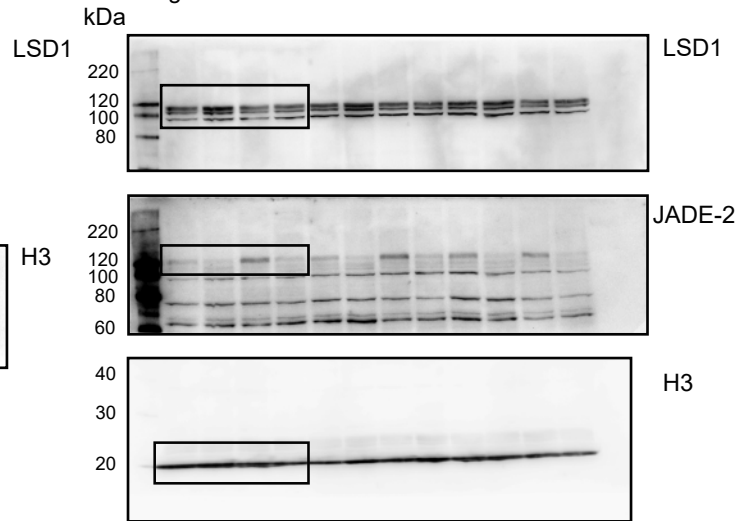


Table S1 - Primers used in this study

Gene Symbol	Gene Name	Forward (5'-3')	Reverse (5'-3')
Quantitative RT-PCR			
<i>36B4</i>	ribosomal protein, large, P0	GCGTCCTGGCATTGTCTGT	GCAAATGCAGATGGATCAGCC
<i>Lsd1</i>	lysine (K)-specific demethylase 1A	ATGGATGTCACACTTCTGGA	CAAGACCTGTTACAACCATG
<i>Pdk4</i>	pyruvate dehydrogenase kinase, isoenzyme 4	CAAGGAGATCTGAATCTCTA	GATAATGTTTGAAGGCTGAC
<i>Atgl</i>	adipose triglyceride lipase (patatin-like phospholipase domain containing 2)	GCCAACGCCACTCACATCTA	GCCTCCTTGGACACCTCAAT
<i>Acadl</i>	acyl-Coenzyme A dehydrogenase, long-chain	AGAACAGATCGAGAAGTTCA	GCGTTCGTTCTTACTCCTTG
<i>Acadm</i>	acyl-Coenzyme A dehydrogenase, medium chain	ATTTGGAAGCTGCTAGTGG	TGGTAACTGAGCCTAGCGAG
<i>Pgc1a</i>	peroxisome proliferative activated receptor, gamma, coactivator 1 alpha	AAGTGTTGAACTCTCTGGAAGT	GGGTTATCTTGGTTGGCTTTATG
<i>Myh7</i>	myosin, heavy polypeptide 7, cardiac muscle, beta	CTCAAGCTGCTCAGCAATCTATTT	GGAGCGCAAGTTTGTATAAAGT
<i>Myh2</i>	myosin, heavy polypeptide 2, skeletal muscle, adult	GAGCAAAGATGCAGGGAAG	TAAGGGTTGACGGTGACACA
<i>Myh1</i>	myosin, heavy polypeptide 1, skeletal muscle, adult	GCATCGAGTGGGAGTTCATT	TGAGCTTCAACCTTGCCTTT
<i>Myh4</i>	myosin, heavy polypeptide 4, skeletal muscle	ACATTATTGGCTGGCTGGAC	ACCCTTCTTCTTGGCACCTT
<i>Myl2</i>	myosin, light polypeptide 2, regulatory, cardiac, slow	TGACCACACAAGCAGAGAGG	CCGTGGGTAAATGATGTGGA
<i>Myl1</i>	myosin, light polypeptide 1	CCCAGCCAACCTAAGGAAG	TGCATTCACCTGTTCTGTCAA
<i>Mylpf</i>	myosin light chain, phosphorylatable, fast skeletal muscle	AGGGAGCTCCAACGTCTTCT	GCGTCGAGTTCCTCATTCTT
<i>Jade1</i>	jade family PHD finger 1	CCCAGCAGCAGTGAGGATT	GATCAGGTCGGTCCATAACA
<i>Jade2</i>	jade family PHD finger 2	CCATCAGCAGCGACAACCTCT	TGAGGGCTTCTTCTGTTCT
<i>Usp28</i>	ubiquitin specific peptidase 28	GAGCTGCAGCAGGACGACT	ATCCTGGATGCCTGTGATTT
<i>Myod1</i>	myogenic differentiation 1	TACAGTGGCGACTCAGATGC	GAGATGCGCTCCACTATGCT
<i>Myog</i>	myogenin	CAGTGAATGCAACTCCCACAGC	CACCCAGCCTGACAGACAATCTC
ChIP-quantitative PCR			
<i>Pdk4</i>	promoter exon 9	CTGGCTAGGAATGCGTGACA GGTGTTCCTCTGAGGATTAC	GATCCCAGGTCGCTAGGACT GCATTCGGGAATTGTCCAT
<i>Atgl</i>	promoter	TGCCAAGCTGTGGGATTGA	AGCCATCTGAGAGACCTGGA
<i>Pgc1a</i>	promoter +100kb	GAGCAGCTCACTGCTTGTGT CACAAACACCTGGCACTCAC	CTCCAGAGATTACGGGAAA CCACTTGCCTCATGCTGACA
<i>Myh7</i>	E-box promoter exon 4 +10kb	GGGTGCCTGGTGTATTGAGT GGGGGAAATGCTTTTAGTGA GCGGGAAGGCATATAGGTAA CCACAATCCCACACCTCTCT	GCCAGGATTAGGGAGCTGA CAGCTCCCACTCCTACCTGA CATCGGGCACAAAACATC ATGCCTGAGCCTGCGTATTT
<i>Jade2</i>	1 2 3 4 5 6	CAAGCCATAGAGACACCCAAC TGTGTCTGTGGCTGGATGA TGGAGGGGAAAGGAAAATAA CATCGCAGTTGGAGGCTATT GGATGGGACAGCTCATTCT TCCCAGATTCATACCAGCTCA	CAGTGGAGTGAAGGGAGAACA CGGCTCTGTTTCCAGATT TTTTTGAAGGCAGGTGGATG CCTGCTGGGAAGATGGTC AGGTTTTTCCTGCTCCACA CACCCCTTTCTCCATTCTT

Table S2 - Mapped read counts in ChIP-seq analysis

Experiment #	Cells	Condition	Antigen	Read counts
1	C2C12	normally differentiated, on day 2	input	16472156
1	C2C12	normally differentiated, on day 2	LSD1	18031920
2	C2C12	normally differentiated, on day 5	input	17298668
2	C2C12	normally differentiated, on day 5	LSD1	15778509
3	C2C12	differentiated with control vehicle, on day 2	input	15068639
3	C2C12	differentiated with control vehicle, on day 2	H3K4me1	17664635
3	C2C12	differentiated with control vehicle, on day 2	H3K4me2	13126558
3	C2C12	differentiated with S2101, on day 2	input	13267750
3	C2C12	differentiated with S2101, on day 2	H3K4me1	10139301
3	C2C12	differentiated with S2101, on day 2	H3K4me2	12139283
4	C2C12	differentiated with control vehicle, on day 2	input	14798951
4	C2C12	differentiated with control vehicle, on day 2	H3	19367010
4	C2C12	differentiated with control vehicle, on day 2	H3K4me3	13074866
4	C2C12	differentiated with S2101, on day 2	input	17021862
4	C2C12	differentiated with S2101, on day 2	H3	15851644
4	C2C12	differentiated with S2101, on day 2	H3K4me3	14256097

Table S3 - 435 LSD1-bound genes upregulated by both inhibitors and LSD1 KD

Gene Symbol	Gene Title
0610010O12Rik	RIKEN cDNA 0610010O12 gene
1200009I06Rik	RIKEN cDNA 1200009I06 gene
1700052N19Rik	RIKEN cDNA 1700052N19 gene
1700112E06Rik	RIKEN cDNA 1700112E06 gene
1810012P15Rik	RIKEN cDNA 1810012P15 gene
1810013D10Rik	RIKEN cDNA 1810013D10 gene
1810014F10Rik	RIKEN cDNA 1810014F10 gene
2310044G17Rik	RIKEN cDNA 2310044G17 gene
2410066E13Rik	RIKEN cDNA 2410066E13 gene
2410076I21Rik	RIKEN cDNA 2410076I21 gene
A930001N09Rik	RIKEN cDNA A930001N09 gene
AA467197	expressed sequence AA467197
Abca2	ATP-binding cassette, sub-family A (ABC1), member 2
Abca3	ATP-binding cassette, sub-family A (ABC1), member 3
Abcd2	ATP-binding cassette, sub-family D (ALD), member 2
Acer3	alkaline ceramidase 3
Acot11	acyl-CoA thioesterase 11
Acss2	acyl-CoA synthetase short-chain family member 2
Adamts1	ADAMTS-like 1
Adamts4	ADAMTS-like 4
Adamts5	ADAMTS-like 5
Adh7	alcohol dehydrogenase 7 (class IV), mu or sigma polypeptide
Adi1	acireductone dioxygenase 1
Adora2b	adenosine A2b receptor
Afap1l2	actin filament associated protein 1-like 2
Aig1	androgen-induced 1
Aldh1l1	aldehyde dehydrogenase 1 family, member L1
Aldh2	aldehyde dehydrogenase 2, mitochondrial
Aldh3a1	aldehyde dehydrogenase family 3, subfamily A1
Aldoc	aldolase C, fructose-bisphosphate
Ampd3	adenosine monophosphate deaminase 3
Aox1	aldehyde oxidase 1
Ap1g2	adaptor protein complex AP-1, gamma 2 subunit
Apobec1	apolipoprotein B mRNA editing enzyme, catalytic polypeptide 1
Apol7a	apolipoprotein L 7a
Aqp1	aquaporin 1
Aqp5	aquaporin 5
Ar	androgen receptor
Areg	amphiregulin
Arhgap18	Rho GTPase activating protein 18
Arhgef3	Rho guanine nucleotide exchange factor (GEF) 3
Armc10	armadillo repeat containing 10
Arrb2	arrestin, beta 2
Artn	artemin
Arvcf	armadillo repeat gene deleted in velo-cardio-facial syndrome
As3mt	arsenic (+3 oxidation state) methyltransferase
Asl	argininosuccinate lyase
Atat1	alpha tubulin acetyltransferase 1
Atl1	atlastin GTPase 1
Atl3	atlastin GTPase 3
Atp6v0e2	ATPase, H ⁺ transporting, lysosomal V0 subunit E2
AU018091	expressed sequence AU018091
Axl	AXL receptor tyrosine kinase
BC046404	cDNA sequence BC046404
BC052040	cDNA sequence BC052040
Bdh2	3-hydroxybutyrate dehydrogenase, type 2
Bdkrb2	bradykinin receptor, beta 2
Best1	bestrophin 1
Bicd1	bicaudal D homolog 1 (Drosophila)

Bid	BH3 interacting domain death agonist
Bik	BCL2-interacting killer
Blnk	B cell linker
Bst2	bone marrow stromal cell antigen 2
Btbd11	BTB (POZ) domain containing 11
C1galt1	core 1 synthase, glycoprotein-N-acetylgalactosamine 3-beta-galactosyltransferase, 1
C1s	complement component 1, s subcomponent
C630004H02Rik	RIKEN cDNA C630004H02 gene
Cacfd1	calcium channel flower domain containing 1
Cacnb2	calcium channel, voltage-dependent, beta 2 subunit
Cadm4	cell adhesion molecule 4
Calcr1	calcitonin receptor-like
Capn5	calpain 5
Car13	carbonic anhydrase 13
Car2	carbonic anhydrase 2
Car3	carbonic anhydrase 3
Car7	carbonic anhydrase 7
Car8	carbonic anhydrase 8
Card10	caspase recruitment domain family, member 10
Cbr2	carbonyl reductase 2
Cck	cholecystokinin
Cd24a	CD24a antigen
Cd55	CD55 antigen
Cda	cytidine deaminase
Cdc42bpg	CDC42 binding protein kinase gamma (DMPK-like)
Cdh1	cadherin 1
Cdk2ap2	CDK2-associated protein 2
Cebpb	CCAAT/enhancer binding protein (C/EBP), beta
Celf5	CUGBP, Elav-like family member 5
Cerk	ceramide kinase
Cgnl1	cingulin-like 1
Ch25h	cholesterol 25-hydroxylase
Chchd10	coiled-coil-helix-coiled-coil-helix domain containing 10
Chd7	chromodomain helicase DNA binding protein 7
Chd8	chromodomain helicase DNA binding protein 8
Chek1	checkpoint kinase 1
Chmp4c	charged multivesicular body protein 4C
Chn2	chimerin (chimaerin) 2
Cklf	chemokine-like factor
Clca5	chloride channel calcium activated 5
Clcn3	chloride channel 3
Cldn7	claudin 7
Cldn9	claudin 9
Clic5	chloride intracellular channel 5
Clip4	CAP-GLY domain containing linker protein family, member 4
Clmn	calmin
Clu	clusterin
Cmb1	carboxymethylenebutenolidase-like (Pseudomonas)
Cobl	cordon-bleu
Cobl1	Cobl-like 1
Coro1a	coronin, actin binding protein 1A
Cox7a1	cytochrome c oxidase, subunit VIIa 1
Cpd	carboxypeptidase D
Creb5	cAMP responsive element binding protein 5
Creld1	cysteine-rich with EGF-like domains 1
Crem	cAMP responsive element modulator
Csf2rb	colony stimulating factor 2 receptor, beta, low-affinity (granulocyte-macrophage)
Cst6	cystatin E/M
Ctnnal1	catenin (cadherin associated protein), alpha-like 1
Ctsb	cathepsin B
Cxcr4	chemokine (C-X-C motif) receptor 4

Cyfp2	cytoplasmic FMR1 interacting protein 2
Cyp26a1	cytochrome P450, family 26, subfamily a, polypeptide 1
Dab2	disabled 2, mitogen-responsive phosphoprotein
Dact2	dapper homolog 2, antagonist of beta-catenin (xenopus)
Dbi	diazepam binding inhibitor
Ddah1	dimethylarginine dimethylaminohydrolase 1
Dennd3	DENN/MADD domain containing 3
Dmxl2	Dmx-like 2
Dntt	Deoxynucleotidyltransferase, terminal
Dock11	dedicator of cytokinesis 11
Dock5	dedicator of cytokinesis 5
Dock8	dedicator of cytokinesis 8
Dock9	dedicator of cytokinesis 9
Dok7	docking protein 7
Dopey2	dopey family member 2
Dpp7	dipeptidylpeptidase 7
Dpy19l3	dpy-19-like 3 (C. elegans)
Dtd1	D-tyrosyl-tRNA deacylase 1 homolog (S. cerevisiae)
Dtna	dystrobrevin alpha
Dtwd2	DTW domain containing 2
E130308A19Rik	RIKEN cDNA E130308A19 gene
Elovl6	ELOVL family member 6, elongation of long chain fatty acids (yeast)
Elovl7	ELOVL family member 7, elongation of long chain fatty acids (yeast)
Eml2	echinoderm microtubule associated protein like 2
Eml5	echinoderm microtubule associated protein like 5
Enpp4	ectonucleotide pyrophosphatase/phosphodiesterase 4
Epb4.115	erythrocyte protein band 4.1-like 5
Epb4.9	erythrocyte protein band 4.9
Ephx4	epoxide hydrolase 4
Epn2	epsin 2
Eps8	epidermal growth factor receptor pathway substrate 8
Ermp1	endoplasmic reticulum metalloproteinase 1
Etfdh	electron transferring flavoprotein, dehydrogenase
Ethe1	ethylmalonic encephalopathy 1
Etl4	enhancer trap locus 4
Exd1	exonuclease 3'-5' domain containing 1
Exoc6	exocyst complex component 6
Eya1	eyes absent 1 homolog (Drosophila)
Ezr	ezrin
F11r	F11 receptor
Fads2	fatty acid desaturase 2
Fam107a	family with sequence similarity 107, member A
Fam55c	family with sequence similarity 55, member C
Fam84b	family with sequence similarity 84, member B
Fdft1	farnesyl diphosphate farnesyl transferase 1
Fetub	fetuin beta
Fez1	fasciculation and elongation protein zeta 1 (zygin I)
Fgd2	FYVE, RhoGEF and PH domain containing 2
Fgl2	fibrinogen-like protein 2
Foxc2	forkhead box C2
Foxred2	FAD-dependent oxidoreductase domain containing 2
Galm	galactose mutarotase
Galnt6	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 6
Galnt7	UDP-N-acetyl-alpha-D-galactosamine: polypeptide N-acetylgalactosaminyltransferase 7
Gbe1	glucan (1,4-alpha-), branching enzyme 1
Gch1	GTP cyclohydrolase 1
Gcnt2	glucosaminyl (N-acetyl) transferase 2, I-branching enzyme
Gdpd1	glycerophosphodiester phosphodiesterase domain containing 1
Gdpd5	glycerophosphodiester phosphodiesterase domain containing 5
Gfra2	glial cell line derived neurotrophic factor family receptor alpha 2
Gja3	gap junction protein, alpha 3

Gm2a	GM2 ganglioside activator protein
Gna14	guanine nucleotide binding protein, alpha 14
Gpm6b	glycoprotein m6b
Gpnmb	glycoprotein (transmembrane) nmb
Gpr133	G protein-coupled receptor 133
Gpr173	G-protein coupled receptor 173
Gramd1b	GRAM domain containing 1B
Grasp	GRP1 (general receptor for phosphoinositides 1)-associated scaffold protein
Grina	glutamate receptor, ionotropic, N-methyl D-aspartate-associated protein 1 (glutamate binding)
Grn	granulin
Gspt2	G1 to S phase transition 2
Gsta4	glutathione S-transferase, alpha 4
Gstm1	glutathione S-transferase, mu 1
Havcr2	hepatitis A virus cellular receptor 2
Hdc	histidine decarboxylase
Heg1	HEG homolog 1 (zebrafish)
Hltf	helicase-like transcription factor
Hnmt	histamine N-methyltransferase
Hoxa3	homeobox A3
Hsd3b7	hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 7
Hspa4l	heat shock protein 4 like
Htr1b	5-hydroxytryptamine (serotonin) receptor 1B
Id2	inhibitor of DNA binding 2
Ier3	immediate early response 3
Ifitm1	interferon induced transmembrane protein 1
Ifitm3	interferon induced transmembrane protein 3
Igfbp5	insulin-like growth factor binding protein 5
Il33	interleukin 33
Il6ra	interleukin 6 receptor, alpha
Insig1	insulin induced gene 1
Insl6	insulin-like 6
Irgm2	immunity-related GTPase family M member 2
Itgb8	integrin beta 8
Itgbl1	integrin, beta-like 1
Kat2b	K(lysine) acetyltransferase 2B
Kbtbd11	kelch repeat and BTB (POZ) domain containing 11
Kcnab3	potassium voltage-gated channel, shaker-related subfamily, beta member 3
Kcnmb2	potassium large conductance calcium-activated channel, subfamily M, beta member 2
Kif13b	kinesin family member 13B
Kif16b	kinesin family member 16B
Kif21a	kinesin family member 21A
Krt80	keratin 80
Lama3	laminin, alpha 3
Lama5	laminin, alpha 5
Lims2	LIM and senescent cell antigen like domains 2
Lmbr1	limb region 1
Lonrf3	LON peptidase N-terminal domain and ring finger 3
Lrba	LPS-responsive beige-like anchor
Lrrc27	leucine rich repeat containing 27
Lrrc8b	leucine rich repeat containing 8 family, member B
Lrrc8d	leucine rich repeat containing 8D
Lrsam1	leucine rich repeat and sterile alpha motif containing 1
Lztr1	leucine-zipper-like transcriptional regulator, 1
Magi3	membrane associated guanylate kinase, WW and PDZ domain containing 3
Manba	mannosidase, beta A, lysosomal
Map1lc3a	microtubule-associated protein 1 light chain 3 alpha
Map3k8	mitogen-activated protein kinase kinase kinase 8
Map4k2	mitogen-activated protein kinase kinase kinase kinase 2
Mapre2	microtubule-associated protein, RP/EB family, member 2
Mapt	microtubule-associated protein tau
Mblac2	metallo-beta-lactamase domain containing 2

Mfap3l microfibrillar-associated protein 3-like
Mfsd6 major facilitator superfamily domain containing 6
Mical3 microtubule associated monooxygenase, calponin and LIM domain containing 3
Mknk2 MAP kinase-interacting serine/threonine kinase 2
Mkrn1 makorin, ring finger protein, 1
Mt2 metallothionein 2
Mtap2 microtubule-associated protein 2
Mtch2 mitochondrial carrier homolog 2 (C. elegans)
Mtss1 metastasis suppressor 1
Naip2 NLR family, apoptosis inhibitory protein 2
Nalcn sodium leak channel, non-selective
Nbeal2 neurobeachin-like 2
Ncald neurocalcin delta
Nceh1 arylacetamide deacetylase-like 1
Ndrg2 N-myc downstream regulated gene 2
Ndrg4 N-myc downstream regulated gene 4
Neb1 nebulin
Nedd9 neural precursor cell expressed, developmentally down-regulated gene 9
Neu1 neuraminidase 1
Nfe2l2 nuclear factor, erythroid derived 2, like 2
Nipal3 NIPA-like domain containing 3
Nkd2 naked cuticle 2 homolog (Drosophila)
Nlr5 NLR family, CARD domain containing 5
Nqo1 NAD(P)H dehydrogenase, quinone 1
Nrn1 neuritin 1
Nrxn3 neurexin III
Nsg1 neuron specific gene family member 1
Nt5e 5' nucleotidase, ecto
Nup210 nucleoporin 210
Obfc2a oligonucleotide/oligosaccharide-binding fold containing 2A
Ociad2 OCIA domain containing 2
Ocln occludin
Odz4 odd Oz/ten-m homolog 4 (Drosophila)
Olfm1 olfactomedin 1
Pag1 phosphoprotein associated with glycosphingolipid microdomains 1
Pcbd1 pterin 4 alpha carbinolamine dehydratase/dimerization cofactor of hepatocyte nuclear factor 1 alpha (TCF1) 1
Pcp4l1 Purkinje cell protein 4-like 1
Pde4b phosphodiesterase 4B, cAMP specific
Pde4dip phosphodiesterase 4D interacting protein (myomegalin)
Pdk4 pyruvate dehydrogenase kinase, isoenzyme 4
Peg3 paternally expressed 3
Perp PERP, TP53 apoptosis effector
Pgpep1 pyroglutamyl-peptidase I
Pi15 peptidase inhibitor 15
Pik3ip1 phosphoinositide-3-kinase interacting protein 1
Pim1 proviral integration site 1
Pkp2 Plakophilin 2
Pla2g2e phospholipase A2, group IIE
Pla2g6 phospholipase A2, group VI
Plcg2 phospholipase C, gamma 2
Plcl2 phospholipase C-like 2
Plekha6 pleckstrin homology domain containing, family A member 6
Plekha7 pleckstrin homology domain containing, family A member 7
Plekha1 pleckstrin homology domain containing, family B (evectins) member 1
Plin2 perilipin 2
Pltp phospholipid transfer protein
Plxdc1 plexin domain containing 1
Plxdc2 plexin domain containing 2
Pmvk phosphomevalonate kinase
Pnpla2 patatin-like phospholipase domain containing 2

Pnpla6	patatin-like phospholipase domain containing 6
Podxl	podocalyxin-like
Pou4f1	POU domain, class 4, transcription factor 1
Ppp1r9a	protein phosphatase 1, regulatory (inhibitor) subunit 9A
Prkag2	protein kinase, AMP-activated, gamma 2 non-catalytic subunit
Prrg4	proline rich Gla (G-carboxyglutamic acid) 4 (transmembrane)
Prrx1	paired related homeobox 1
Pzca	prostate stem cell antigen
Ptgds	prostaglandin D2 synthase (brain)
Ptgis	prostaglandin I2 (prostacyclin) synthase
Ptgs1	prostaglandin-endoperoxide synthase 1
Ptp4a3	protein tyrosine phosphatase 4a3
Ptpkb	protein tyrosine phosphatase-like (proline instead of catalytic arginine), member b
Ptpn22	protein tyrosine phosphatase, non-receptor type 22 (lymphoid)
Qpct	glutaminyl-peptide cyclotransferase (glutaminyl cyclase)
Qser1	glutamine and serine rich 1
Rab20	RAB20, member RAS oncogene family
Rab27b	RAB27b, member RAS oncogene family
Rab3il1	RAB3A interacting protein (rabin3)-like 1
Rab3ip	RAB3A interacting protein
Rab43	RAB43, member RAS oncogene family
Rabepk	Rab9 effector protein with kelch motifs
Ralb	v-ral simian leukemia viral oncogene homolog B (ras related)
Ralgapa1	Ral GTPase activating protein, alpha subunit 1
Ralgs1	Ral GEF with PH domain and SH3 binding motif 1
Ralgs2	Ral GEF with PH domain and SH3 binding motif 2
Rapgef3	Rap guanine nucleotide exchange factor (GEF) 3
Rarb	retinoic acid receptor, beta
Rasa3	RAS p21 protein activator 3
Rassf2	Ras association (RalGDS/AF-6) domain family member 2
Rassf4	Ras association (RalGDS/AF-6) domain family member 4
Rbm47	RNA binding motif protein 47
Rcan3	regulator of calcineurin 3
Reep2	receptor accessory protein 2
Repin1	replication initiator 1
Rftn1	raftlin lipid raft linker 1
Rgs2	regulator of G-protein signaling 2
Rhpn2	rhopilin, Rho GTPase binding protein 2
Rnasel	ribonuclease L (2', 5'-oligoadenylate synthetase-dependent)
Rnf157	ring finger protein 157
Ropn1l	ropporin 1-like
Rp2h	retinitis pigmentosa 2 homolog (human)
Runx1t1	runt-related transcription factor 1; translocated to, 1 (cyclin D-related)
Scd1	stearoyl-Coenzyme A desaturase 1
Scn5a	sodium channel, voltage-gated, type V, alpha
Scrn1	secernin 1
Sema3d	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3D
Sema5a	sema domain, seven thrombospondin repeats (type 1 and type 1-like), transmembrane domain (TM) and short cytoplasmic domain, (semaphorin) 5A
Serpnb6b	serine (or cysteine) peptidase inhibitor, clade B, member 6b
Serping1	serine (or cysteine) peptidase inhibitor, clade G, member 1
Sfmbt2	Scm-like with four mbt domains 2
Sft2d2	SFT2 domain containing 2
Sh3bgr	SH3-binding domain glutamic acid-rich protein
Sigirr	single immunoglobulin and toll-interleukin 1 receptor (TIR) domain
Slc16a13	solute carrier family 16 (monocarboxylic acid transporters), member 13
Slc1a5	solute carrier family 1 (neutral amino acid transporter), member 5
Slc24a6	solute carrier family 24 (sodium/potassium/calcium exchanger), member 6
Slc25a23	solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 23
Slc25a30	solute carrier family 25, member 30
Slc27a1	solute carrier family 27 (fatty acid transporter), member 1

Slc2a3 solute carrier family 2 (facilitated glucose transporter), member 3
 Slc2a6 solute carrier family 2 (facilitated glucose transporter), member 6
 Slc31a2 solute carrier family 31, member 2
 Slc48a1 solute carrier family 48 (heme transporter), member 1
 Slc7a7 solute carrier family 7 (cationic amino acid transporter, y⁺ system), member 7
 Slc9a2 solute carrier family 9 (sodium/hydrogen exchanger), member 2
 Slc9a3r1 solute carrier family 9 (sodium/hydrogen exchanger), member 3 regulator 1
 Snx10 sorting nexin 10
 Sord sorbitol dehydrogenase
 Spint1 serine protease inhibitor, Kunitz type 1
 Spn sialophorin
 St6gal1 beta galactoside alpha 2,6 sialyltransferase 1
 Stap2 signal transducing adaptor family member 2
 Stard9 START domain containing 9
 Stk32b serine/threonine kinase 32B
 Strbp spermatid perinuclear RNA binding protein
 Stx11 syntaxin 11
 Svip small VCP/p97-interacting protein
 Sybu syntabulin (syntaxin-interacting)
 Syngri1 synaptogyrin 1
 Syt11 synaptotagmin XI
 Tbc1d4 TBC1 domain family, member 4
 Tcf4 transcription factor 4
 Tdrkh tudor and KH domain containing protein
 Tek endothelial-specific receptor tyrosine kinase
 Tgfr1 transforming growth factor, beta receptor I
 Tgm2 transglutaminase 2, C polypeptide
 Thbd thrombomodulin
 Thsd4 thrombospondin, type I, domain containing 4
 Tlcd1 TLC domain containing 1
 Tik1 tousled-like kinase 1
 Tlr3 toll-like receptor 3
 Tlr4 toll-like receptor 4
 Tm7sf2 transmembrane 7 superfamily member 2
 Tm7sf3 transmembrane 7 superfamily member 3
 Tmem106c transmembrane protein 106C
 Tmem14a transmembrane protein 14A
 Tmem25 transmembrane protein 25
 Tmem64 transmembrane protein 64
 Tmem71 transmembrane protein 71
 Tnfaip2 tumor necrosis factor, alpha-induced protein 2
 Tnfrsf22 tumor necrosis factor receptor superfamily, member 22
 Tom111 target of myb1-like 1 (chicken)
 Tox2 TOX high mobility group box family member 2
 Tpd52 tumor protein D52
 Tpd52l1 tumor protein D52-like 1
 Trib2 tribbles homolog 2 (Drosophila)
 Trim16 tripartite motif-containing 16
 Trim7 tripartite motif-containing 7
 Tslp thymic stromal lymphopoietin
 Tspan11 tetraspanin 11
 Tspan15 tetraspanin 15
 Ttc19 tetratricopeptide repeat domain 19
 Ttc21b tetratricopeptide repeat domain 21B
 Tuft1 tuftelin 1
 Txnrd3 thioredoxin reductase 3
 Uap1l1 UDP-N-acetylglucosamine pyrophosphorylase 1-like 1
 Ube2l6 ubiquitin-conjugating enzyme E2L 6
 Uchl1 ubiquitin carboxy-terminal hydrolase L1
 Unc45a unc-45 homolog A (C. elegans)
 Vat1 vesicle amine transport protein 1 homolog (T. californica)

Wbp2	WW domain binding protein 2
Wnt4	wingless-related MMTV integration site 4
Xdh	xanthine dehydrogenase
Xiap	X-linked inhibitor of apoptosis
Xpo7	exportin 7
Yip2	Yip1 domain family, member 2
Ypel1	yippee-like 1 (Drosophila)
Zbtb20	zinc finger and BTB domain containing 20
Zdhhc2	zinc finger, DHHC domain containing 2
Zfp467	zinc finger protein 467
Zfp605	zinc finger protein 605
Znrf2	zinc and ring finger 2
