Supplemental Figure Legends

Fig. S1. FXR binding peaks at the *Lsd1* gene. (A) FXR binding peaks (red bars) detected within the *Lsd1* gene from mouse liver ChIP-seq analysis (Lee et al., Hepatology, 2012). (B) Sequences for 16 IR1 motifs that are potential FXR response elements detected within 50 Kb the *Lsd1* gene are presented.

Fig. S2. Partially purified FXR and RXRα used in in the gel mobility shift assays. Flag-RXR and 3flag-FXR were expressed in Cos-1 cells and purified by M2 agarose. Eluted proteins were visualized by Coomassie blue staining. Approximate concentrations of proteins were estimated according to bovine serum albumin standards.

Fig. S3. Gel mobility shift assays using mouse liver nuclear extracts. γ-32P-labeled oligonucleotide probe containing the IR motif #6 was incubated with 10 μg of mouse liver nuclear extracts, 2 μg poly-dIdC and 0.25 μg of sonicated salmon sperm DNA, and 2.5 μg of BSA. For antibody (Ab) supershift experiments (lanes 2-5) and competitor experiments (lanes, 6-11), Ab (0.4 μg) or double-stranded unlabeled oligonucleotides containing the IR motif #6 (WT) or mutated (Mut) IR1 motif (1, 10, 30 ng) were preincubated with nuclear extracts for 10 min before adding the probe.

Fig. S4. Hepatic protein levels of LSD1 detected by IHC. (A, B) WT mice and FXR-KO mice were treated with GW4064 for 3 h (A) or fed 0.5 % CA-supplemented chow for 6 h (B) and hepatic LSD1 protein levels were detected by IHC.

Fig. S5. CDCA treatment increases LSD1/SHP co-localization. Immunofluorescent detection of LSD1 (green) and SHP (red) images showing co-localization (Merge) in Hepa1c1c7 cells treated with CDCA for 3 h.

Fig. S6. Cell-based luciferase reporter assays: effects of overexpression or downregulation of LSD1 on *CYP7A1*-luc activity. HepG2 cells were transfected with plasmids as indicated and treated with 50 μM CDCA overnight and luciferase activity was measured. The values for firefly luciferase activities were normalized by dividing by the β-galactosidase activities. The mean and SEM (n=3) are plotted.

Fig. S7. Effects of downregulation of SHP on *CYP7A1 and CYP8B1* mRNA levels in HepG2 cells. HepG2 cells were infected with Ad-shSHP or control virus and 60 h later, cells were treated with vehicle or 50 μM CDCA for 8 h. The mRNA levels of indicated genes were measured by q-RTPCR (SEM, n=3).

Fig. S8. Effects of downregulation of *LSD1* on occupancy of SHP and histone H3K4-me3 levels at *CYP7A1 and CYP8B1* genes. HepG2 cells were infected with Ad-shLSD1 or control virus and 60 h later, cells were treated with 50 μM CDCA or vehicle for 8 h and ChIP assays were performed. Three independent assays were performed (SEM, n=3).

Fig. S9. Hepatic protein levels of LSD1 detected by IHC. Mice were infected with Ad-shLSD1 or control virus and 6 days later, mice were fed a 0.5% CA-supplemented diet for 6 h. Hepatic LSD1 protein levels were detected by IHC. The scale bar is100 μm.

Fig. S10. Effects of downregulation of *Lsd1* on mRNA levels of *SHP and LSD1* after 6 h of CA feeding. Mice were infected with Ad-shSHP or control virus and 6 days later, mice were fed a 0.5 % CA-supplemented diet for 6 h. *Shp and Lsd1* mRNA levels were measured by q-RTPCR (SEM, n=3 mice).

Fig. S11. Effects of downregulation of *Lsd1* on mRNA levels of *SHP and LSD1* after 6 days of CA feeding. Mice were infected with Ad-shSHP or control virus and 6 days later, mice were fed 0.5 % CA-supplemented diet for 6 days. *Shp and Lsd1* mRNA levels were measured by q-RTPCR (SEM, n=3 mice).

Fig. S12. Effects of downregulation of *Lsd1* on mRNA levels of BA transporters. Mice were infected with Ad-shLSD1 or control virus for 6 days and then were fed CA chow for 6 days. The mRNA levels of the indicated genes involved in BA transport were measured by q-RTPCR. The mean and SEM (n=3) are plotted and statistical significance was measured using Student's t-test. *p<0.05.

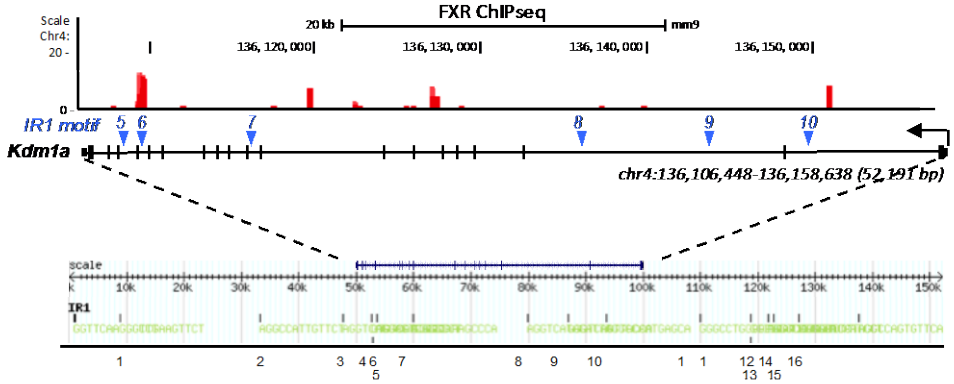
Fig. S13. Effects of downregulation of *Lsd1* on activation of ERK and JNK kinases in mouse liver. Mice were tail vein injected with Ad-shLSD1 or control Ad-Empty virus and 6 days later, mice were fed normal chow (-CA) or 0.5% CA-supplemented chow (+CA) for 6 days and livers were pooled from 3 mice. Liver extracts were prepared, and protein levels of activated phosphorylated ERK (p-ERK) or JNK (p-JNK) and total levels of ERK (t-ERK) and JNK (t-JNK) were detected by IB.

Fig. S14. Effects of downregulation of SHP or Prox1 on occupancy of LSD1 at *Cyp7a1* gene. (A) Primary mouse hepatocytes were infected with Ad-shSHP or control virus and 60 h later, cells were treated with CDCA or vehicle and ChIP assays were performed. (B) Endogenous Prox1 in hepatocytes was downregulated using siRNA and then, cells were treated with CDCA or vehicle and ChIP assays were performed. Reduced SHP and Prox1 protein levels are shown below. Three independent combined shRNA or siRNA/ChIP experiments were performed and the mean and SEM (n=3) are plotted.

Supplemental Figures

Fig. S1

A



B

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IR1-2	AGGCCATTGTTCT	Chr4: 136089711-136089723	+68928 - +68916
IR1-3	AGGTCAGGAGTCT	Chr4: 136104273-136104285	+54366 - +54354
IR1-4	GTGTCAATGGCCT	Chr4: 136109173-136109185	+49466 - +49454
IR1-5	AGGTCAAAAACTT	Chr4: 136109343-136109355	+49296 - +49284
IR1-6	AGGCCTCAGGCCT	Chr4: 136110004-136110016	+48635 - +48623
IR1-7	GGGCCAAAGCCCA	Chr4: 136116410-136116422	+42229 - +42217
IR1-8	AGGTCATAGATTT	Chr4: 136136367-136136379	+22272 - +22260
IR1-9	GGGTCAGTTACCA	Chr4: 136143415-136143427	+15224 - +15212
IR1-10	AGGCCAATGAGCA	Chr4: 136150082-136150094	+8557 - +8545
IR1-11	GGGCCTGGGGCCT	Chr4: 136166384-136166396	-7745 – -7757
IR1-12	GGGCCATTGTCTA	Chr4: 136175088-136175100	-16449 – -16461
IR1-13	GGGCCAGAGTTCC	Chr4: 136175158-136175170	-16519 – -16531
IR1-14	AGGTCACGGGCTT	Chr4: 136178133-136178145	-19494 – -19506
IR1-16	AGGCCAGAATCCT	Chr4: 136179215-136179227	-20576 – -20588
IR1-15	GGGGCACAATCCT	Chr4: 136183463-136183475	-24824 – -24836
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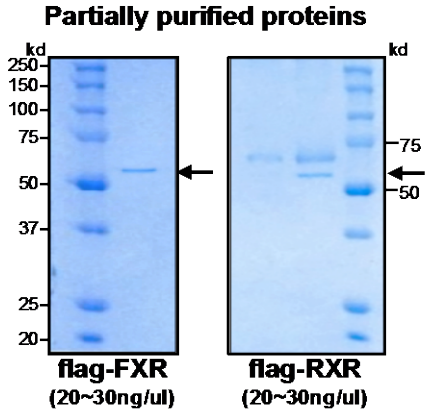
Fig. S2



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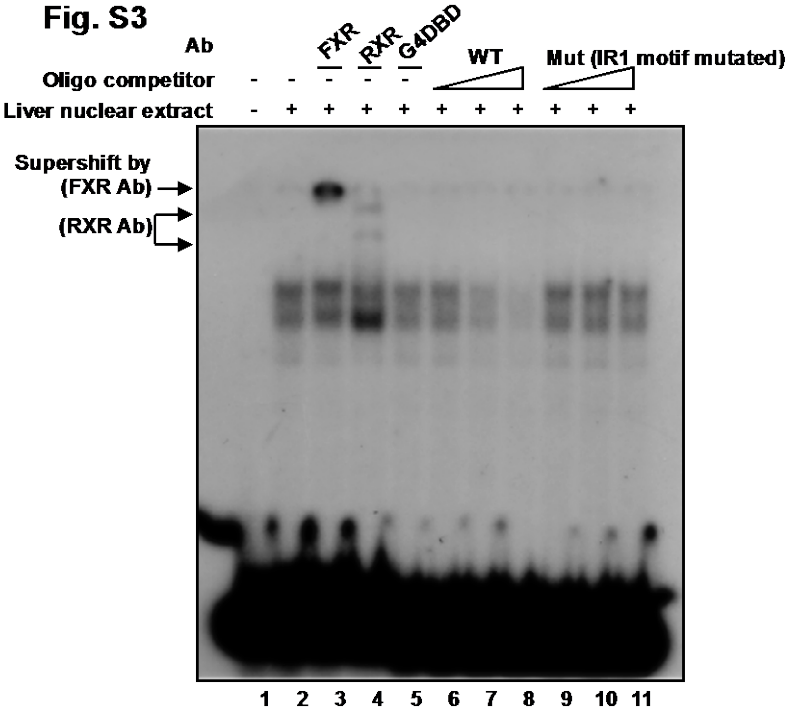

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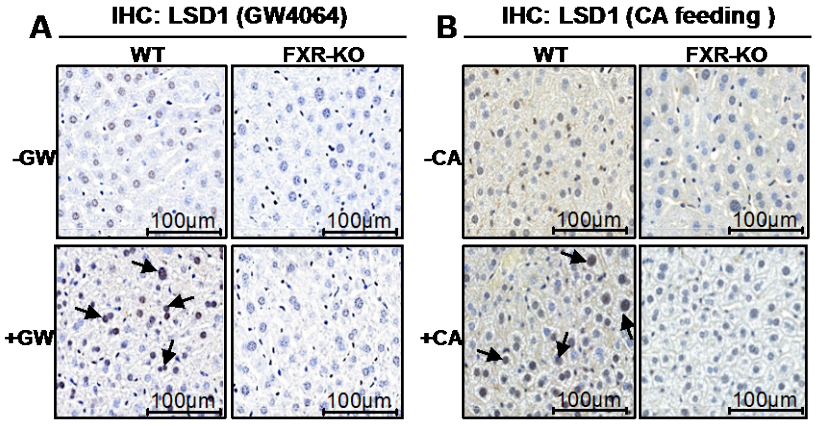

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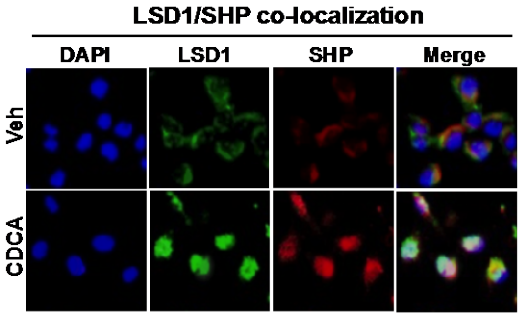

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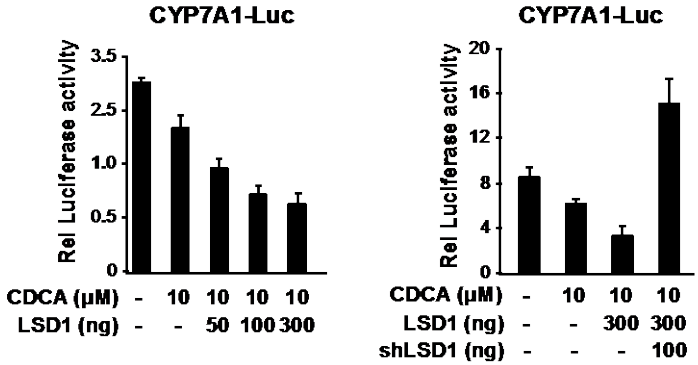

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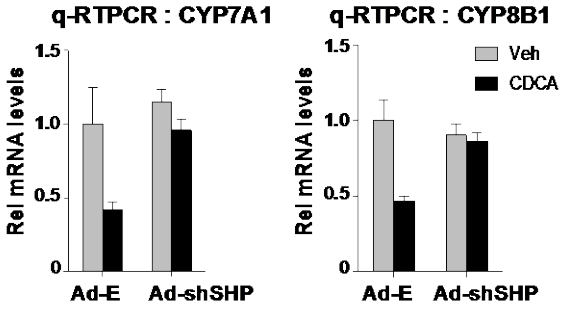

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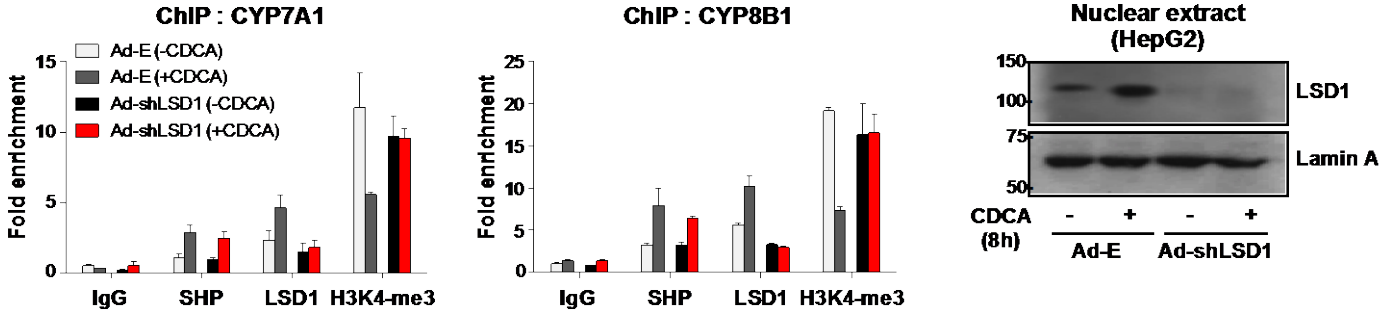

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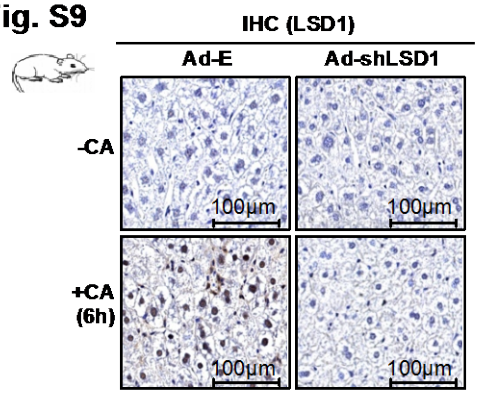

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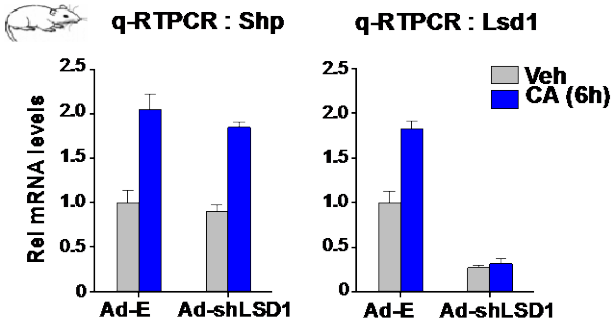

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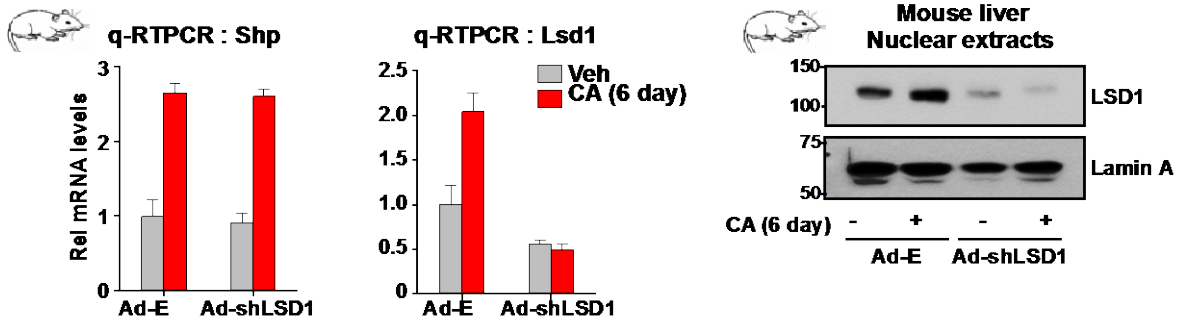
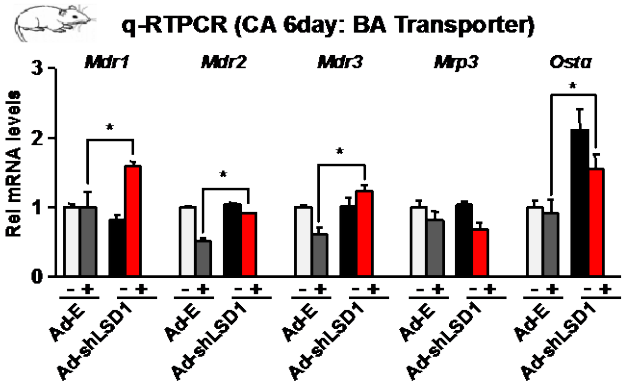


Fig. S12



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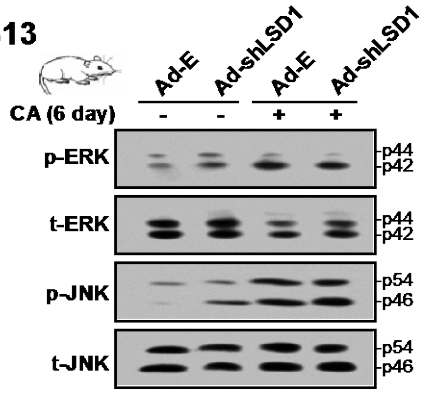

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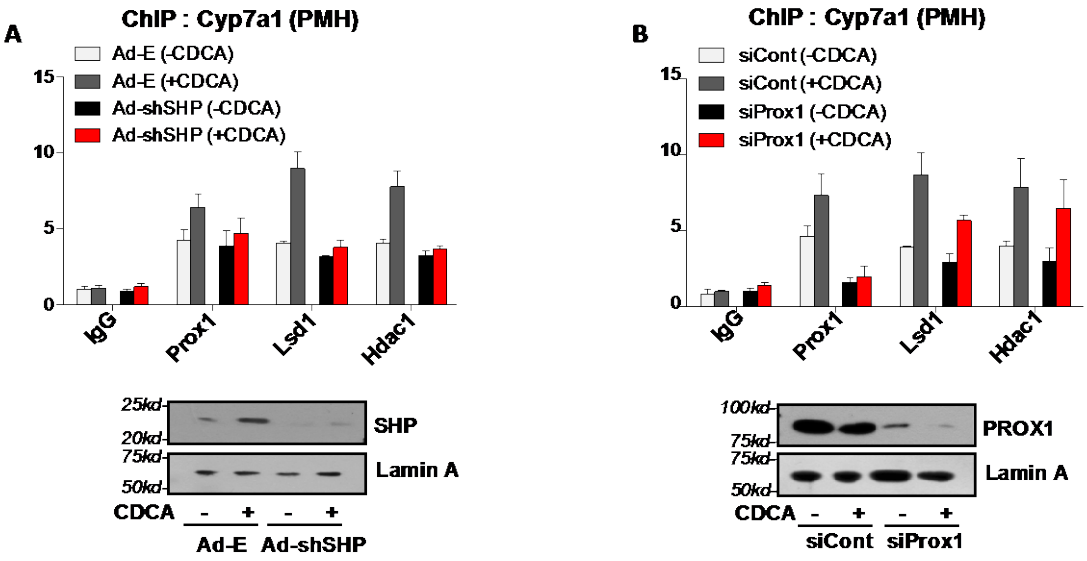

Fig. S15

Primers used in this study (ChIP and q-RTPCR)

	Purpose	Definition	Sense Primer	Anti-sense Primer
human	ChIP	CYP7A1	GCCCATCTTAAACAGGTT	TCCACAGGTATCAGAAGT
human	ChIP	CYP8B1	CAGCCAGCCTCAGGAGAAATG	CCCCGACCCAGCGACCAGCCA
human	mRNA	36B4	TGCTGAACATGCTCAAC	GTCGAACACCTGCTGGATGAC
human	mRNA	CYP7A1	TGGGCATCGCAAGCAAA	CTTTCATTGCTTCTGGGTTCCTA
human	mRNA	CYP8B1	TTCGCTTCTGCTATTACATCTT	TCCTGCTCCTTGTCCTTC
mouse	ChIP	Cyp7a1	ATATGCACAGGACCATGATC	CTTTGGTAGGTGAGCTCTTC
mouse	ChIP	Cyp8b1	AAGCATGGGGATGTGTTCAC	CAAACTTGCGGAACTCCATG
mouse	ChIP	Ntcp	TACCTCCTCCCTGATGCCTTTC	TGCGTCTGCAGCTTGGATTTA
mouse	ChIP	Shp	ACAGCAGCGATAAGCCACTT	GCCTGGGACTGCTGTTTCTA
mouse	mRNA	36B4	CCCTGAAGTGCTCGACATCA	TGCGGACACCCTCCAGAA
mouse	mRNA	Bsep	CAATGTTCAGTTCCTCCGTTCA	TTTGGTGTTGTCCCCSTSCTTG
mouse	mRNA	Cyp27a1	GACAACCTCCTTTGGGACTTAC	GTGGTCTCTTATTGGGTACTTGC
mouse	mRNA	Cyp2b10	TCCTGACCAGTTCCTGGATG	CTGGAGGATGGACGTGAAGAA
mouse	mRNA	Cyp3a11	CGCCTCTCCTTGCTGTCACA	CTTTGCCTTCTGCCTCAAGT
mouse	mRNA	Cyp7a1	AACGGGTTGATTCCATACCTGG	GTGGACATATTTCCCCATCAGTT
mouse	mRNA	Cyp7b1	GACGATCCTGAAATAGGAGCACA	AATGGTGTTTGCTAGAGAGGCC
mouse	mRNA	Cyp8b1	GAATCTAACCAGGCCATGCT	AGGAGCTGGCACCTAGACT
mouse	mRNA	IL1b	GGACCCATATGAGCTGAAAGCT	TGTCGTTGCTTGGTTCTCCTT
mouse	mRNA	Lsd1	AGCAGCCTGTTTCCCAGACA	TGCAATGTGCGATTCCTGAT
mouse	mRNA	Mdr1	CTGGTGTGCTCATAGTTG	CCTAATCTTGTGTATCTGTCTT
mouse	mRNA	Mrp2	TATCCCCGGGAAATCTGTTC	TAACCAACATTCTCCGCGC
mouse	mRNA	Mrp3	AAGAGGAGATAGCAGAGA	ATACAGGAGGCAGATAGA
mouse	mRNA	Mrp4	CACCATTGCTCACAGACT	CAAGACATACGGCTCATCA
mouse	mRNA	Oatp1	CCTGGAGCAGCAATATGGAAA	CCAAGGCATACTGGAGGCAA
mouse	mRNA	Ostα	TGGACCCTGGAAGACATA	TAACCACTGATAAGGCTGAG
mouse	mRNA	Ostβ	ATCTTGATGACTCCATAATG	GTCTTTCTCTTTCAACTCA
mouse	mRNA	Shp	TCTGCAGGTCGTCCGACTAT	CAGGCAGTGGCTGTGAGAT
mouse	mRNA	Sult2a1	AGGACCACGACTCATAACCTCCCA	CCGAGTGACCCTGGATTCTTCACA
mouse	mRNA	Ugt1a1	TCTGAGCCCTGCATCTATCTG	CCCCAGAGGCGTTGACATA
mouse	Pre-mRNA	LSD1 (In1-Ex2)	AAGTCTGAAAGCAATTAGTT	ATTCATCTTCTGAGAGGTT