Supplemental Information

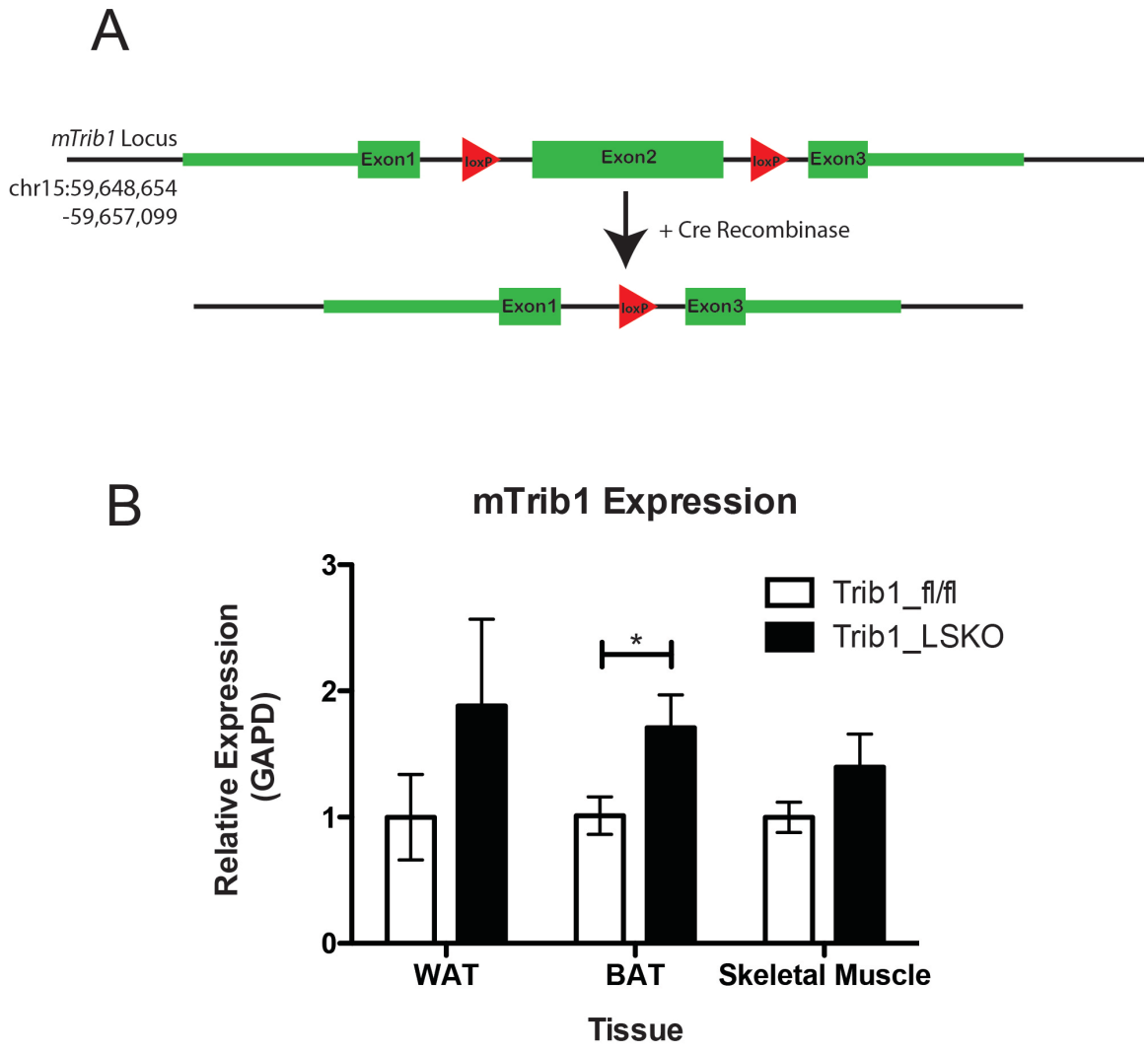

Figure S1. Gene Targeting Approach in Trib1_LSKO mice. (A) Design of the conditional floxed allele is shown. Mice were generated with loxP sites flanking the second exon of *Trib1*. Details of the design of the Trib1 mice may be found at http://www.taconic.com/10265. (B) *mTrib1* message levels were assessed in other metabolic tissues such as white adipose tissue (WAT), brown adipose tissue (BAT), and skeletal muscle in both Trib1_fl/fl and Trib1_LSKO mice.

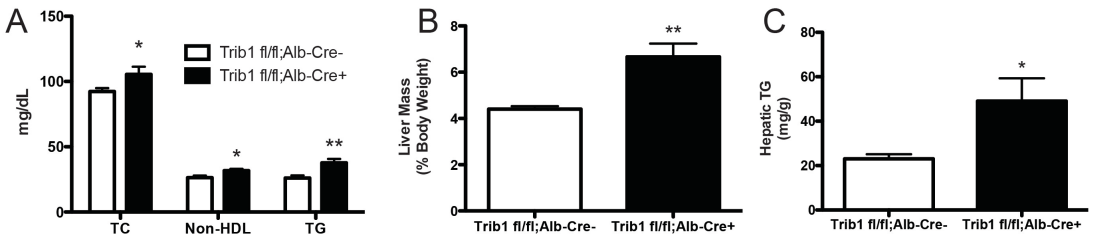

Figure S2. Trib1 fl/fl ; Alb-Cre + have same plasma and hepatic lipid profile as Trib1_LSKO mice. (A) Plasma TC, Non-HDL, and TG from Trib1 fl/fl;Alb-Cre – and + mice show significant increases in all 3 groups (n=10). (B) Liver mass as a percentage of body mass of Trib1 fl/fl;Alb-Cre + mice is increased over Cre- control littermates (n=5). (C) Hepatic TG content from 20mg liver homogenate is increased in Trib1 fl/fl'Alb-Cre + mice as compared to Cre- control littermates (n=5). Error bars are S.E., statistical significance measured by unpaired two-tailed Student's T-Test, * = $p \leq 0.05$, ** = $p \leq 0.01$.

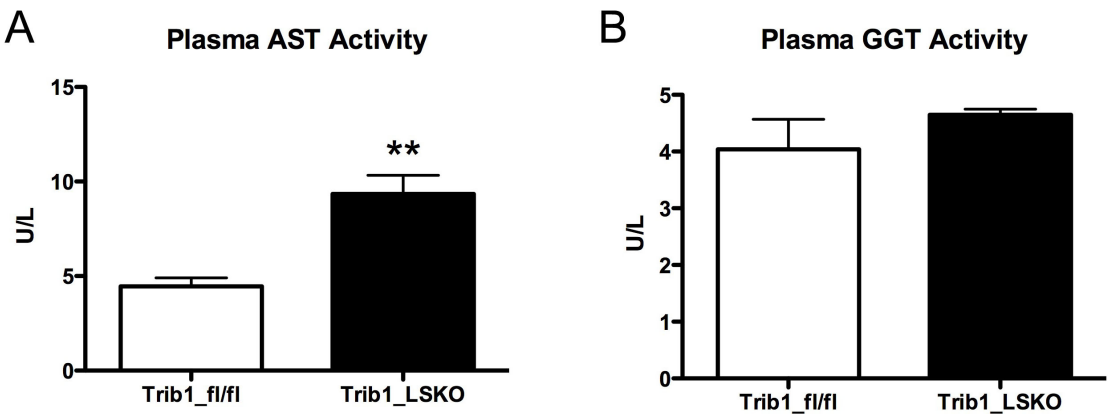

Figure S3: Circulating levels of additional liver enzymes (ASTs and GGTs) in Trib1_LSKO mice. Circulating levels of ASTs (A) and GGTs (B) were measured in plasma from 4-hour fasted Trib1_fl/fl or Trib1_LSKO mice 4 weeks after virus injection. Values were obtained using commercially available kits (Sigma). ** indicates a p-value ≤ 0.01.

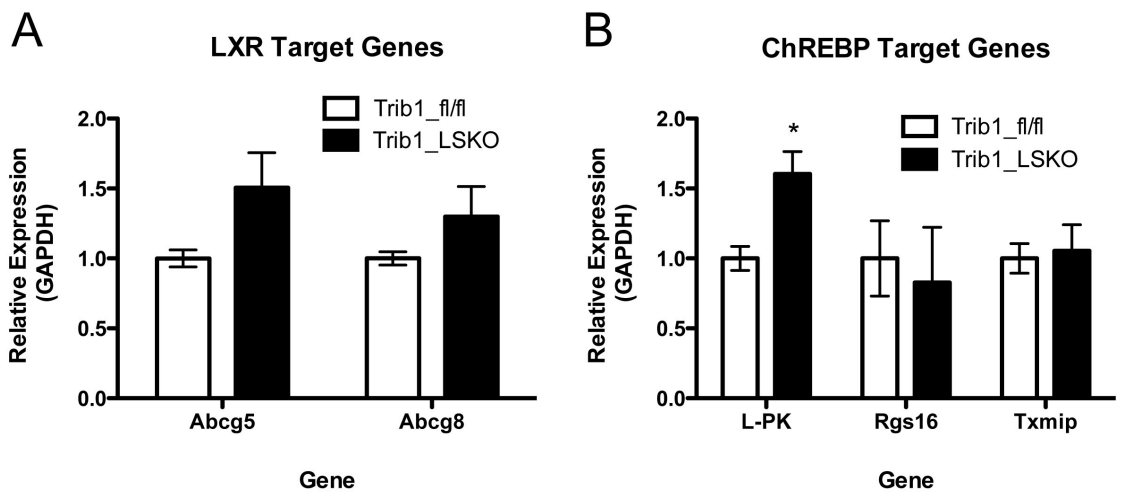

Figure S4: Hepatic Expression of LXR and ChREBP target genes in Trib1 WT and LSKO mice. Hepatic expression of downstream targets of LXR (A) and ChREBP (B) were measured in livers of 4-hour fasted Trib1_fl/fl and Trib1_LSKO mice 4-weeks after virus administration. qRT-PCR was performed using commercially available TaqMan assays (Life Tech). Transcript levels are normalized to the *Gapd* housekeeping gene, and values are relative to the Trib1_fl/fl group which was set to 1. * indicates a *p*-value ≤ 0.05.

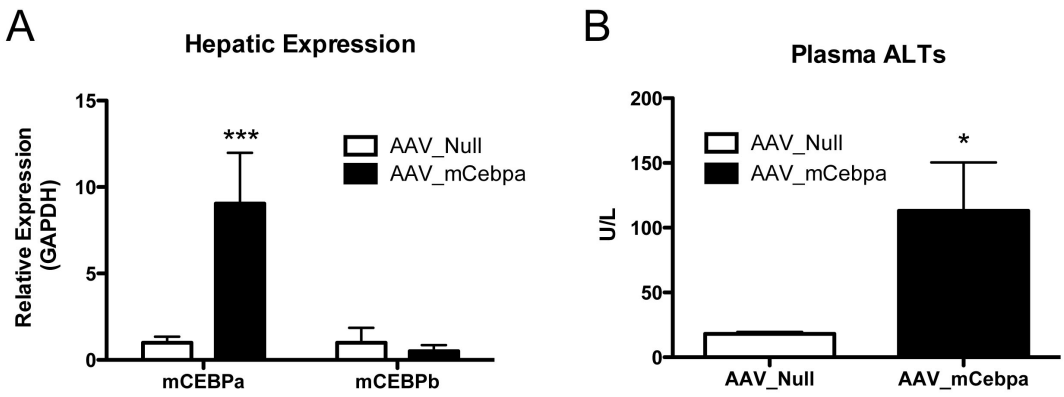

Figure S5. Hepatic overexpression of mCebpa by AAV8-TBG. (A) Message levels of *mCebpa* and *mCebpb* from livers of AAV_Null and AAV-mCebpa mice 2 weeks post-administration of virus, as measured by TaqMan qRT-PCR. (B) Plasma ALTs were also measured in the same mice after a 4-hour fast. All plasma readings were obtained as described in the main methods section.

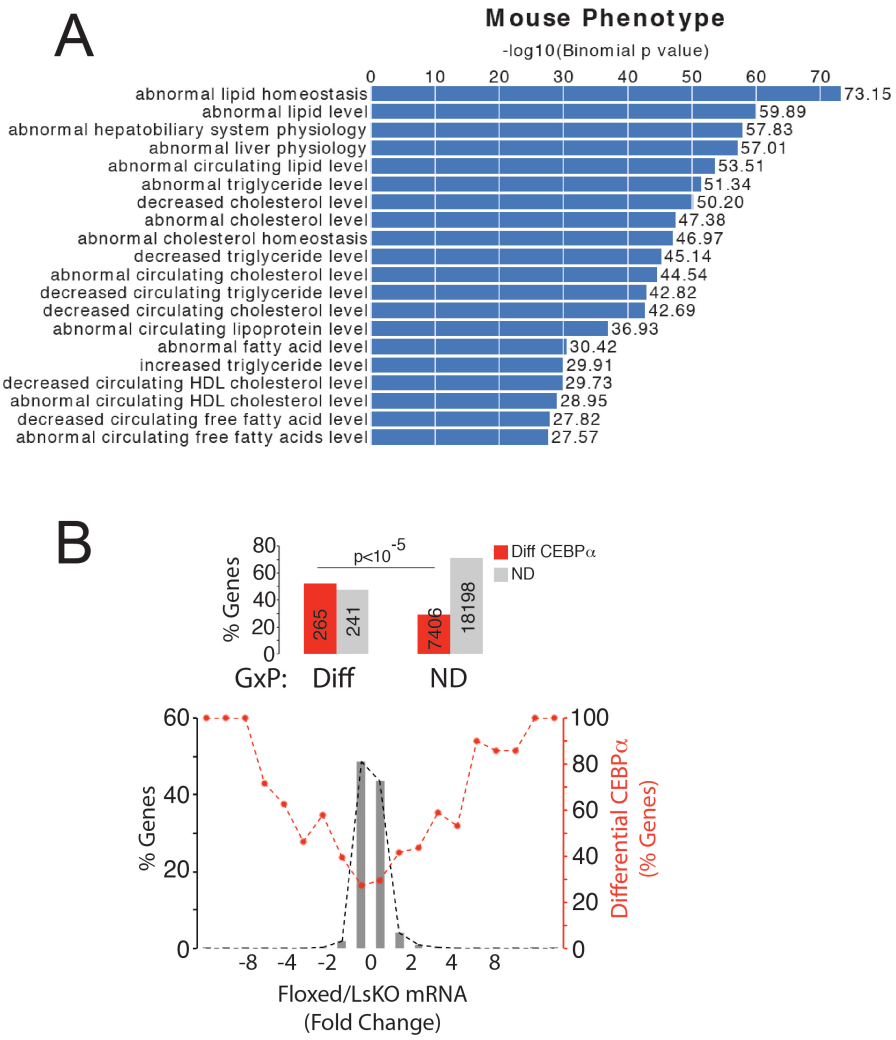

Figure S6. Pathway analysis and correlation with gene expression of C/EBPa ChIP-Seq data from Trib1_fl/fl and Trib1_LSKO mice. (a) Pathway analysis of the strongest 5000 peaks from the Trib1_LSKO mice shows enrichment for lipid homeostasis and both circulating lipids and hepatic lipid content in the C/EBPα hepatic cistrome. (B) There is a highly significant correlation ($p<10^{-5}$) between differential C/EBPα binding and gene expression using, as determined from C/EBPα ChIP-Seq and microarray data from Trib1_fl/fl and Trib1_LSKO mice.

Table S1. Identification of differential C/EBPα binding clusters. Listed below are the genomic coordinates (mm9) of differential C/EBPα binding Clusters (minimum 4 differential peaks) within 100kb of TSS in Trib1_LSKO mice.

Chr.	Region Coord.	Gene_Symbol	distance to TSS	# of Differential Peaks per cluster
chr1	chr1:145721301-145854786	Rgs2	-63236	11
chr15	chr15:59523894-59583564	Trib1	-72785	10
chr15	chr15:22952456-23067009	Cdh18	43515	10
chr18	chr18:55069972-55148190	Zfp608	-40753	10
chr3	chr3:57267420-57457890	Commd2	-92951	9
chr13	chr13:20185634-20297513	Elmo1	59198	9
chr3	chr3:57267420-57457890	Wwtr1	-17177	9
chr3	chr3:57267420-57457890	Wwtr1	-17143	9
chr2	chr2:135610157-135695611	Plcb4	85319	8
chr15	chr15:59645369-59684779	Gm19510	38560	8
chr13	chr13:41425994-41535852	Nedd9	26553	8
chr16	chr16:84995801-85153004	App	-99550	7
chr16	chr16:96026414-96119708	1600002D24Rik	-77623	7
chr5	chr5:72601332-72644883	Commd8	63685	7
chr9	chr9:42097958-42129643	Sc5d	41417	7
chr5	chr5:72601332-72644883	Atp10d	28540	7
chr10	chr10:23947992-23991348	Moxd1	26348	7
chr15	chr15:25756575-25797478	Fam134b	4008	7
chr15	chr15:59332595-59429275	Trib1	-99273	6
chr9	chr9:42292842-42317696	Tecta	97257	6
chr14	chr14:101917083-101985575	Commd6	-88359	6
chr5	chr5:91991600-92070094	Parm1	84122	6
chr16	chr16:77642135-77694162	Mir99a	68968	6
chr16	chr16:77642135-77694162	Mirlet7c-1	68247	6
chr18	chr18:12010136-12113357	Cables1	63964	6
chr11	chr11:105387003-105450112	Tanc2	-32742	6
chr9	chr9:42292842-42317696	Tbcel	24960	6
chr16	chr16:77642135-77694162	Mir125b-2	21631	6
chr6	chr6:7625503-7643331	Asns	-8765	6
chr7	chr7:126055148-126126342	2310008H09Rik	91618	5
chr7	chr7:126055148-126126342	Iqck	91457	5
chr7	chr7:126055148-126126342	2310008H09Rik	91233	5
chr7	chr7:126055148-126126342	2310008H09Rik	91233	5
chr17	chr17:27987450-28140354	Snrpc	86871	5
chr16	chr16:21241761-21339682	Ephb3	85854	5
chr2	chr2:60597006-60683603	Rbms1	-79191	5
chr17	chr17:27987450-28140354	Uhrf1bp1	70451	5
chr9	chr9:7560277-7571447	Mmp10	63503	5
chr4	chr4:61469117-61534287	Mup19	58444	5
chr1	chr1:123166794-123186848	Insig2	-52336	5
chr7	chr7:126055148-126126342	Gprc5b	-47980	5
chr7	chr7:126055148-126126342	Gprc5b	-47980	5
chr15	chr15:83943486-83964160	Pnpla3	-44422	5
chr8	chr8:109474865-109496086	Sntb2	25826	5
chr11	chr11:90044188-90132097	Mmd	-22647	5
chr17	chr17:27987450-28140354	Taf11	19233	5
chr15	chr15:83943486-83964160	Sult4a1	17639	5
chr17	chr17:27987450-28140354	Anks1	17618	5
chr9	chr9:7560277-7571447	Mmp8	7434	5

chr16	chr16:21241761-21339682	A830060N17	-6224	5
chr9	chr9:7560277-7571447	Mmp27	-5595	5
chr4	chr4:61469117-61534287	Mup5	5488	5
chr7	chr7:80480856-80570623	Rgma	5334	5
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chr5	chr5:23504956-23575044	Fam126a	3499	5
chrX	chrX:103322958-103359676	Tlr13	2704	5
chr15	chr15:83943486-83964160	Pnpla5	218	5
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chr3	chr3:128982492-129017160	Pitx2	96991	4
chr11	chr11:28806331-28893698	Efemp1	96810	4
chr10	chr10:33848373-33859933	Bet3l	96751	4
chr9	chr9:86532572-86554174	Prss35	-93060	4
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chrX	chrX:97860210-97896013	P2ry4	87903	4
chr11	chr11:35532289-35590249	Rars	-86761	4
chr7	chr7:140781325-140860401	Bccip	-80152	4
chr7	chr7:140781325-140860401	Uros	-80115	4
chr11	chr11:32264431-32290912	Ubtd2	-77700	4
chrX	chrX:97860210-97896013	Arr3	77276	4
chr18	chr18:4252288-4345363	Mtpap	-76764	4
chr8	chr8:38060672-38121785	Dlc1	75732	4
chr2	chr2:145659246-145713982	Rin2	74763	4
chr3	chr3:84541353-84548278	Tmem154	74702	4
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chr3	chr3:132874396-132922886	Ppa2	-74438	4
chr10	chr10:33848373-33859933	Dse	-73204	4
chr9	chr9:58510751-58526088	2410076I21Rik	-70947	4
chr2	chr2:134478615-134590547	Tmx4	64724	4
chr9	chr9:123033833-123088567	Cdcp1	-63956	4
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chr4	chr4:120145611-120271919	Gm8439	-52584	4
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chr19	chr19:21472537-21536047	Gda	-42859	4
chr2	chr2:145659246-145713982	Naa20	-42362	4
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chr7	chr7:28003505-28023878	BC024978	32892	4
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chr1	chr1:120237477-120277262	Clasp1	-28265	4
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chr4	chr4:84265679-84332163	Bnc2	-22069	4
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chr3	chr3:132874396-132922886	Arhgef38	788	4
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