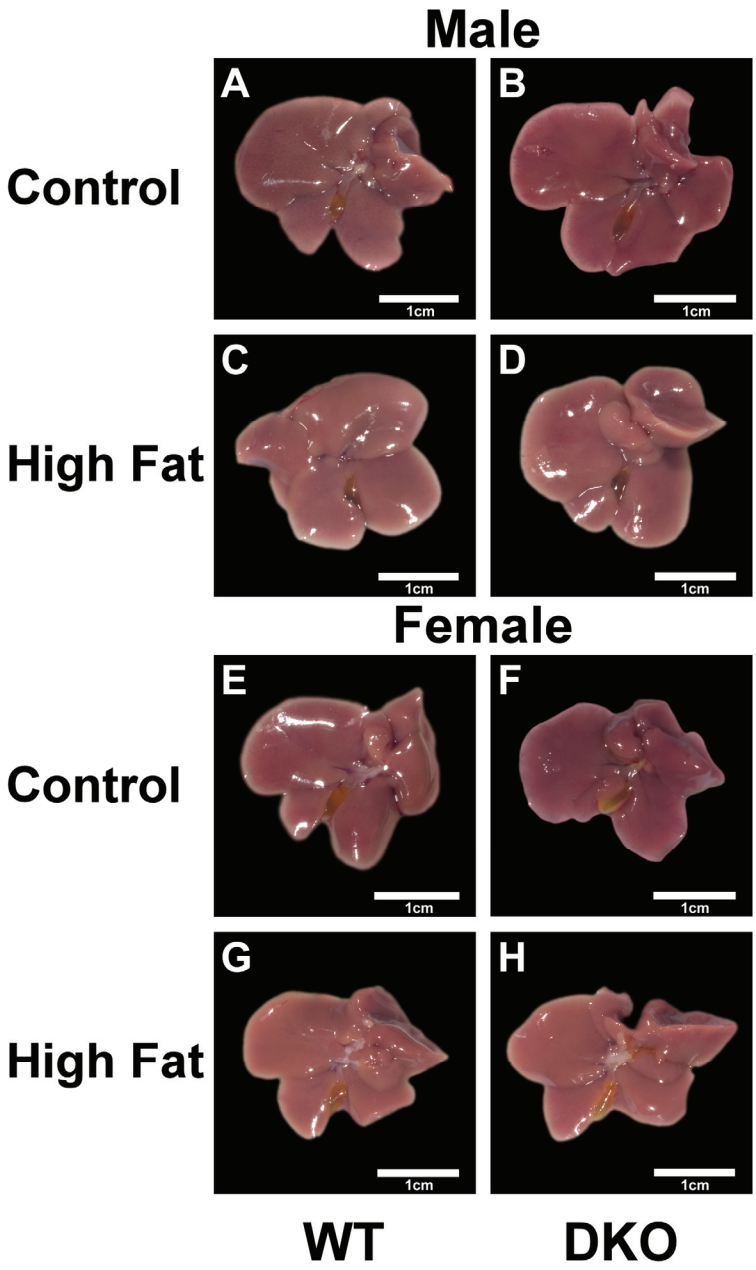
SUPPLEMENTARY DATA

Supplemental TABLE S1. Complete fatty acid profile of control-diet and high fat diet. Fat content and fatty acid compositions of control chow (#B12450b, Research Diets, New Brunswick, NJ) and high fat diet (HFD, # D12451, Research Diets, New Brunswick, NJ) were taken from the DIO Series Fatty Acid Profile, Open Source Diets website (Research Diets, Inc., New Brunswick, NJ). Values are in (g/kg).

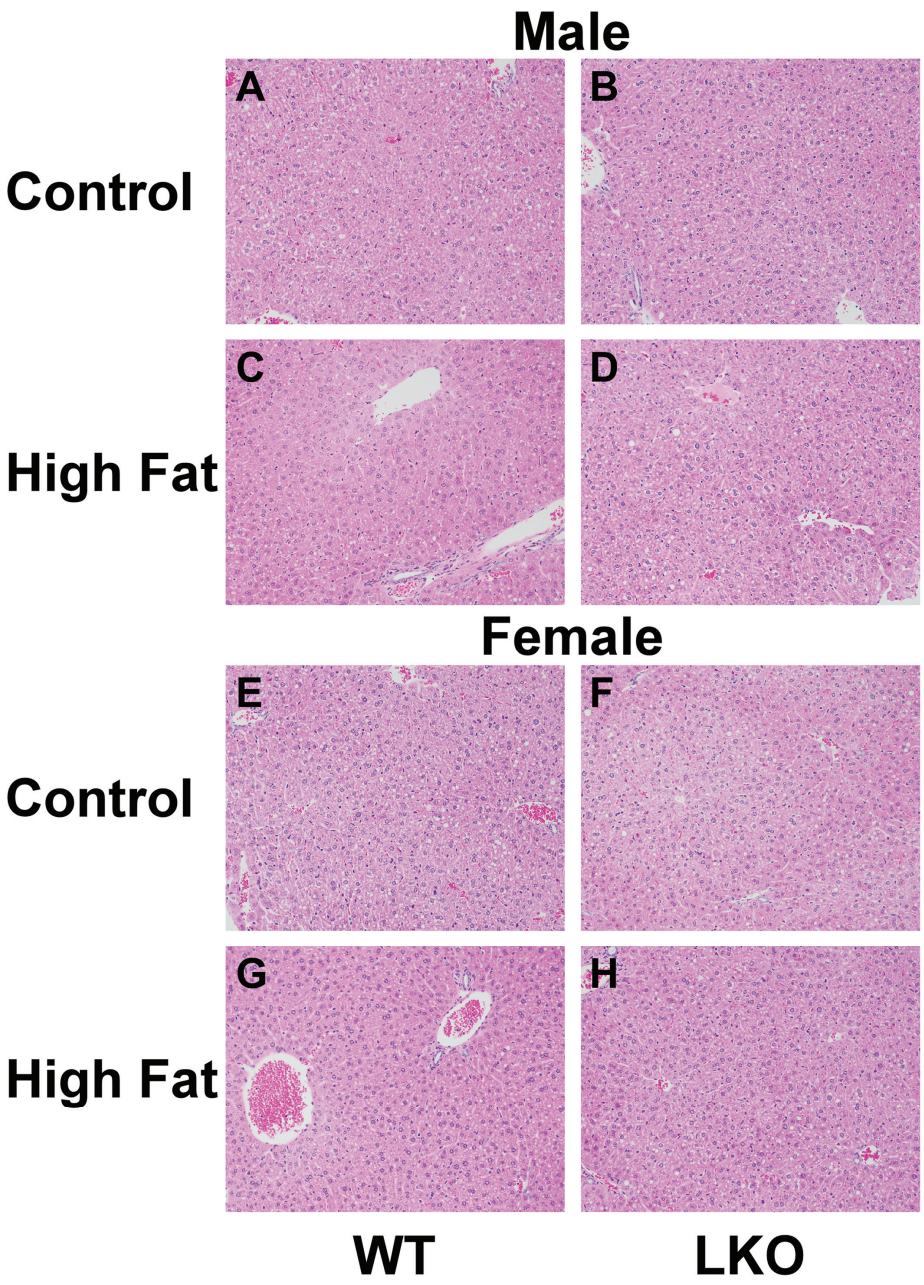
COMPOSITION (g/kg)	D12450B	D12451
Lard	20	177.5
Soybean Oil	25	25
Total	**45**	**202.5**
C2, Acetic	0	0
C4, Butyric	0	0
C6, Caproic	0	0
C8, Caprylic	0	0
C10, Capric	0	0.1
C12, Lauric	0	0.2
C14, Myristic	0.2	2
C14:1, Myristoleic	0	0
C15, Pentadecylic	0	0.1
C16, Palmitic	6.5	36.9
C16:1, Palmitoleic	0.3	2.4
C16:2, Hexadecadienoic	0	0
C16:3, Hexadecatrienoic	0	0
C16:4, Hexadecatetraenoic	0	0
C17, Margaric	0.1	0.7
C17:1, Heptadecenoic	0	0
C18, Stearic	3.1	19.8
C18:1, Oleic	12.6	64.4
C18:2, Linoleic	18.3	56.7
C18:3, Linolenic	2.2	4.3
C18:4, Stearidonic	0	0
C20, Arachidic	0	0.3
C20:1, Gondoic	0.1	1.1
C20:2, Eicosadienoic	0.2	1.4
C20:3, Eicosatrienoic	0	0.2
C20:4, Arachidonic	0.1	0.5
C20:5, Eicosapentaenoic	0	0
C21:5, Heneicosapentaenoic	0	0
C22, Behenic	0	0
C22:1, Erucic	0	0
C22:4, Clupanodonic	0	0

Supplemental TABLE S2. Effect of *Fabp1* gene ablation (LKO) and high-fat diet (HFD) on serum lipid profile in female versus male mice. All conditions were as described in legend to Fig. 1 except that serum lipid composition was determined as described in Methods. Values represent average ± means ± SEM (n=8). By ANOVA $^{\#}$ = P ≤ 0.05 high-fat diet (HFD) vs control diet (CO); * = P ≤ 0.05 LKO versus WT on same diet; $^{\wedge}$ = P ≤ 0.05 female vs male of same genotype and diet.

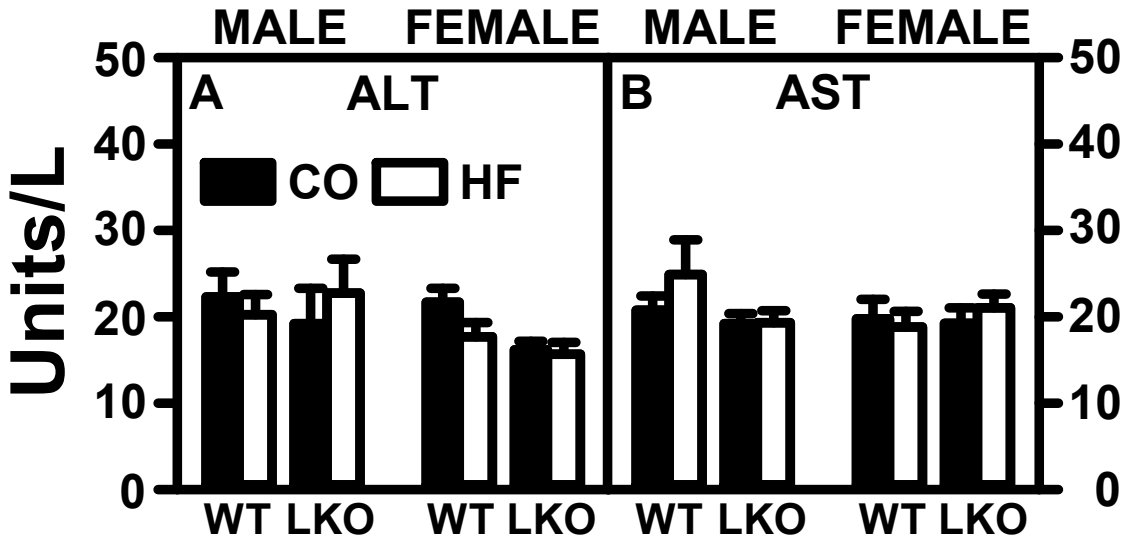
mmol/L	MALE				FEMALE			
	WT		LKO		WT		LKO	
	CO	HFD	CO	HFD	CO	HFD	CO	HFD
Triacylglycerol	0.83±0.07	0.90±0.13	1.19±0.12	1.10±0.06	0.53±0.10$^{\wedge}$	0.45±0.08$^{\wedge}$	0.41±0.06$^{\wedge}$	0.40±0.05$^{\wedge}$
Free Cholesterol	0.66±0.09	0.64±0.05	0.49±0.05	0.42±0.02*	0.24±0.02$^{\wedge}$	0.23±0.02$^{\wedge}$	0.38±0.02*$^{\wedge}$	0.20±0.03$^{\#\wedge}$
Cholesteryl Ester	1.26±0.05	1.25±0.03	1.15±0.02	1.38±0.05$^{\#}$	0.87±0.06$^{\wedge}$	0.91±0.03$^{\wedge}$	0.71±0.05$^{\wedge}$	0.82±0.05$^{\wedge}$
Phospholipid	3.48±0.17	3.08±0.11$^{\#}$	3.06±0.11*	3.11±0.08	2.06±0.10$^{\wedge}$	1.85±0.04$^{\#\wedge}$	1.81±0.03*$^{\wedge}$	1.74±0.05$^{\wedge}$



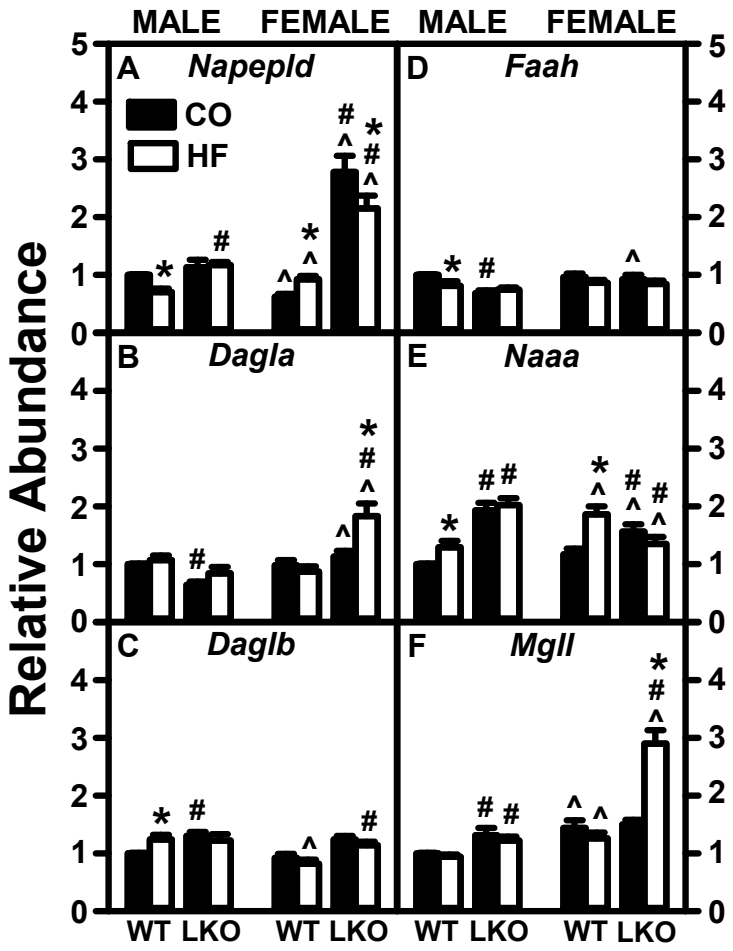
SUPPLEMENTAL FIGURE S1. ***Fabp1*** **gene ablation (LKO) and impact of high-fat diet (HFD) on liver gross morphology in female versus male mice.** Male (**Panels A-D**) and female (**Panels E-H**) wild-type (WT) and *Fabp1* null (knockout; LKO) mice on a C57BL/6N background were pair-fed control (10 kcal%) or high-fat diet (HFD, 45 kcal%) as described in Methods. At the end of the dietary study, mice were euthanized, livers remove, washed with ice-cold PBS, and photographed as detailed in Methods. White bars in each panel represent 1 cm. **Panel A,C,E,G:** WT mice; **Panel B,D,F,H:** LKO mice. **Panel A,B,E,F:** Control diet; **Panel C,D,G,H:** High-fat diet.



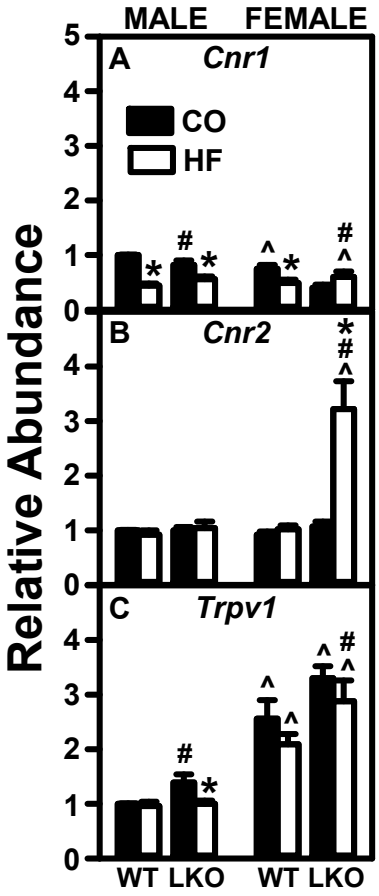
SUPPLEMENTAL FIGURE S2. Effect of *Fabp1* gene ablation (LKO) and pair-fed high-fat diet (HFD) liver histology in female and male mice. Male (**Panels A-D**) and female (**Panels E-H**) wild-type (WT) and *Fabp1* null (knockout; LKO) mice on a C57BL/6N background were pair-fed as in legend to Supplemental Fig. 1. At the end of the dietary study, livers were removed, fixed, sections cut, and H&E stained for histology as described in Methods. Representative histochemical microscopic images were taken as follows: **Panel A,C,E,G:** WT mice; **Panel B,D,F,H:** DKO mice. **Panel A,B,E,F:** Control diet; **Panel C,D,G,H:** Phytol diet.



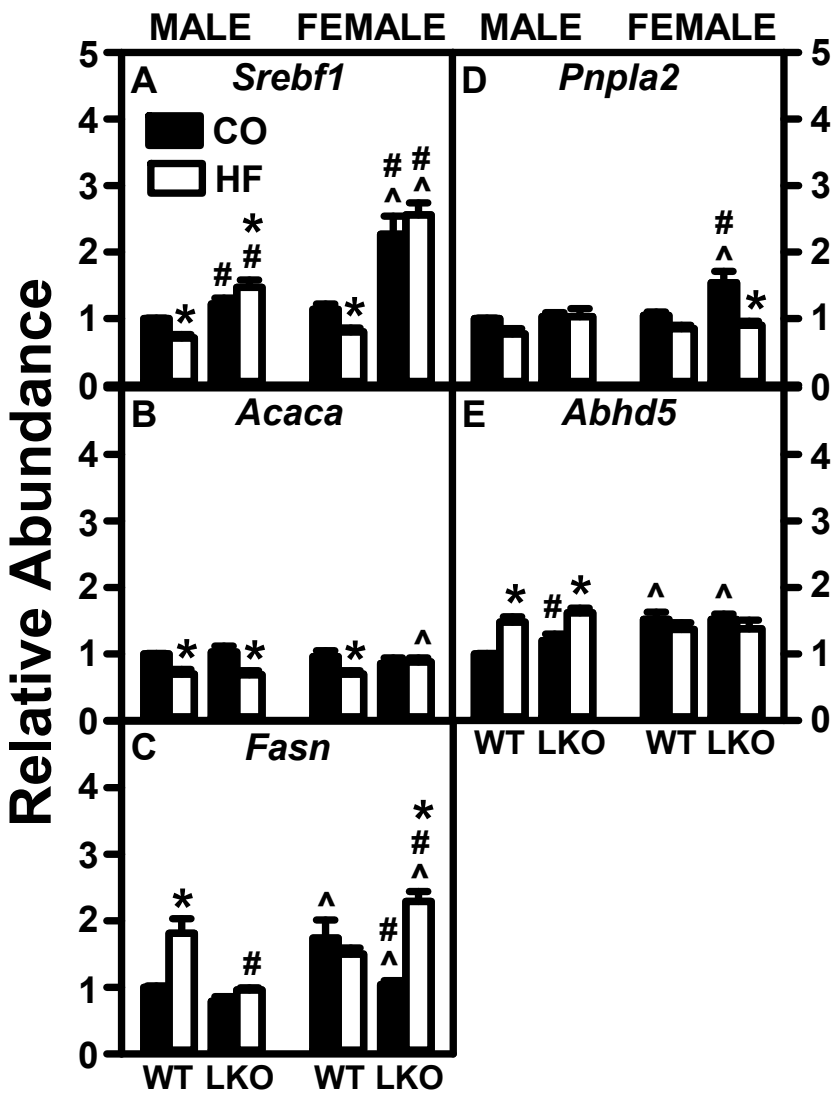
SUPPLEMENTAL FIGURE S3. Impact of *Fabp1* Gene Ablation (LKO) on Serum Enzyme Markers of Hepatotoxicity in Control- and High Fat Fed (HFD) Male and Female Mice. Male and female wild-type (WT) and *Fabp1* null (knockout; LKO) mice on a C57BL/6N background were pair-fed control-diet (**black bars**, CO) or high-fat diet (**open bars**, HFD) as described in Methods. At the end of the dietary study, serum was collected and activities of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) determined therein as described in Methods. Panels A: AST. Panels B, ALT. Values represent the mean ± SEM (n=7). By ANOVA * = $P \leq 0.05$ high-fat diet (HFD) vs control diet (CO); $^{\#}$ = $P \leq 0.05$ LKO versus WT on same diet; $^{\wedge}$ = $P \leq 0.05$ female vs male of same genotype and diet.



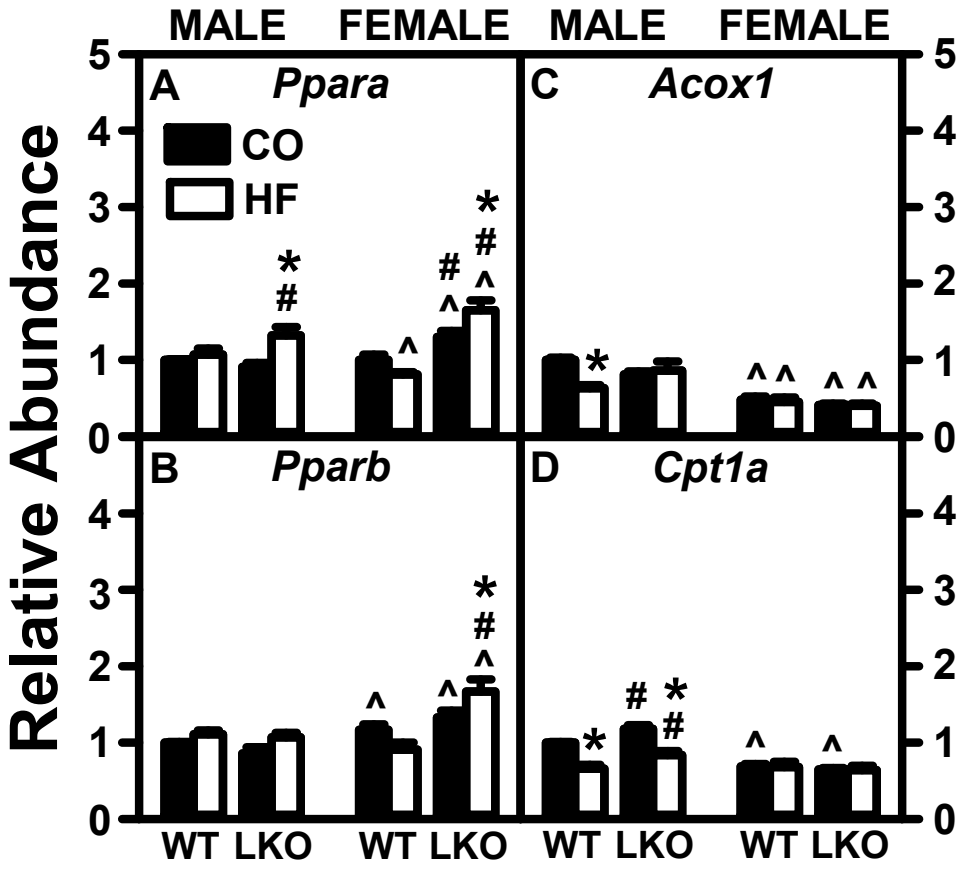
SUPPLEMENTAL FIGURE S4. ***Fabp1*** **gene ablation (LKO) differentially alters the ability of high fat diet (HFD) to impact liver levels of mRNAs encoding proteins of endocannabinoid synthesis and degradation.** Male and female WT and FABP1 LKO mice on a C57BL/6N background were pair-fed a control (**black bars**, CO) or high-fat diet (**open bars**, HFD) as described in Methods. All conditions were as described in Figure 4 except that QrtPCR was used as described in Materials and Methods to determine mRNA levels of: (A) *Napepld*, (B) *Dagla*, (C) *Daglb*, (D) *Faah*, (E) *Naaa*, and (F) *Mgll*. Levels of mRNA were normalized to an internal control (18S RNA), values compared to male WT set to 1, and results expressed as the relative ratio of each protein in high fat to control diet. Mean ± SEM (n = 8). By ANOVA * = $P \leq 0.05$ high-fat diet (HFD) vs control diet (CO); $^{\#}$ = $P \leq 0.05$ LKO versus WT on same diet; $^{\wedge}$ = $P \leq 0.05$ female vs male of same genotype and diet.



SUPPLEMENTAL FIGURE S5. ***Fabp1*** **gene ablation (LKO) selectively enhances the ability of high fat diet (HFD) to increase hepatic levels of mRNAs encoding endocannabinoid receptors.** Male and female WT and FABP1 LKO mice on a C57BL/6N background were pair-fed a control (**black bars**, CO) or high-fat diet (**open bars**, HFD) as described in Methods. All conditions were as described in Figure 4 except that QrtPCR was used as described in Materials and Methods to determine mRNA levels of: (A) *Cnr1*, (B) *Cnr2*, and (C) *Trpv1*. Levels of mRNA were normalized to an internal control (18S RNA), values compared to male WT set to 1, and results expressed as the relative ratio of each protein in high fat to control diet. Mean ± SEM (n = 8). By ANOVA * = $P \leq 0.05$ high-fat diet (HFD) vs control diet (CO); $^{\#}$ = $P \leq 0.05$ LKO versus WT on same diet; $^{\wedge}$ = $P \leq 0.05$ female vs male of same genotype and diet.



SUPPLEMENTAL FIGURE S6. Impact of *Fabp1* gene ablation (LKO) on ability of high fat diet (HFD) to impact hepatic mRNA levels encoding proteins involved in *de novo* lipogenesis. All conditions were as in Figure 4 except that QrtPCR was performed to determine mRNA levels of (A) *Srebpf1*, (B) *Acaca*, (C) *Fasn*, (D) *Pnpla2*, and (E) *Abhd5* as described in Materials and Methods. Levels of mRNA were normalized to an internal control (18S RNA), values compared to male WT set to 1, and results expressed as the relative ratio of each protein in high fat to control diet. Mean ± SEM (n = 8). By ANOVA * = $P \leq 0.05$ high-fat diet (HFD) vs control diet (CO); $^{\#}$ = $P \leq 0.05$ LKO versus WT on same diet; $^{\wedge}$ = $P \leq 0.05$ female vs male of same genotype and diet.



SUPPLEMENTAL FIGURE S7. **Effect of *Fabp1* gene ablation (LKO) to modify the ability of high fat diet (HFD) to alter hepatic levels of mRNAs encoding proteins involved in fatty acid oxidation.** Male and female WT and FABP1 LKO mice on a C57BL/6N background were pair-fed a control (**black bars**, CO) or high-fat diet (**open bars**, HFD) as described in Methods. All conditions were as in Figure 4 except that QrtPCR was performed to determine mRNA levels of (A) *Ppara*, (B) *Pparb*, (C) *Acox1*, and (D) *Cpt1a* as described in Materials and Methods. Levels of mRNA were normalized to an internal control (18S RNA), values compared to male WT set to 1, and results expressed as the relative ratio of each protein in high fat to control diet. Mean ± SEM (n = 8). By ANOVA * = $P \leq 0.05$ high-fat diet (HFD) vs control diet (CO); $^{\#}$ = $P \leq 0.05$ LKO versus WT on same diet; $^{\wedge}$ = $P \leq 0.05$ female vs male of same genotype and diet.