

Supplementary Table 1. Primer sequences used for real-time PCR.

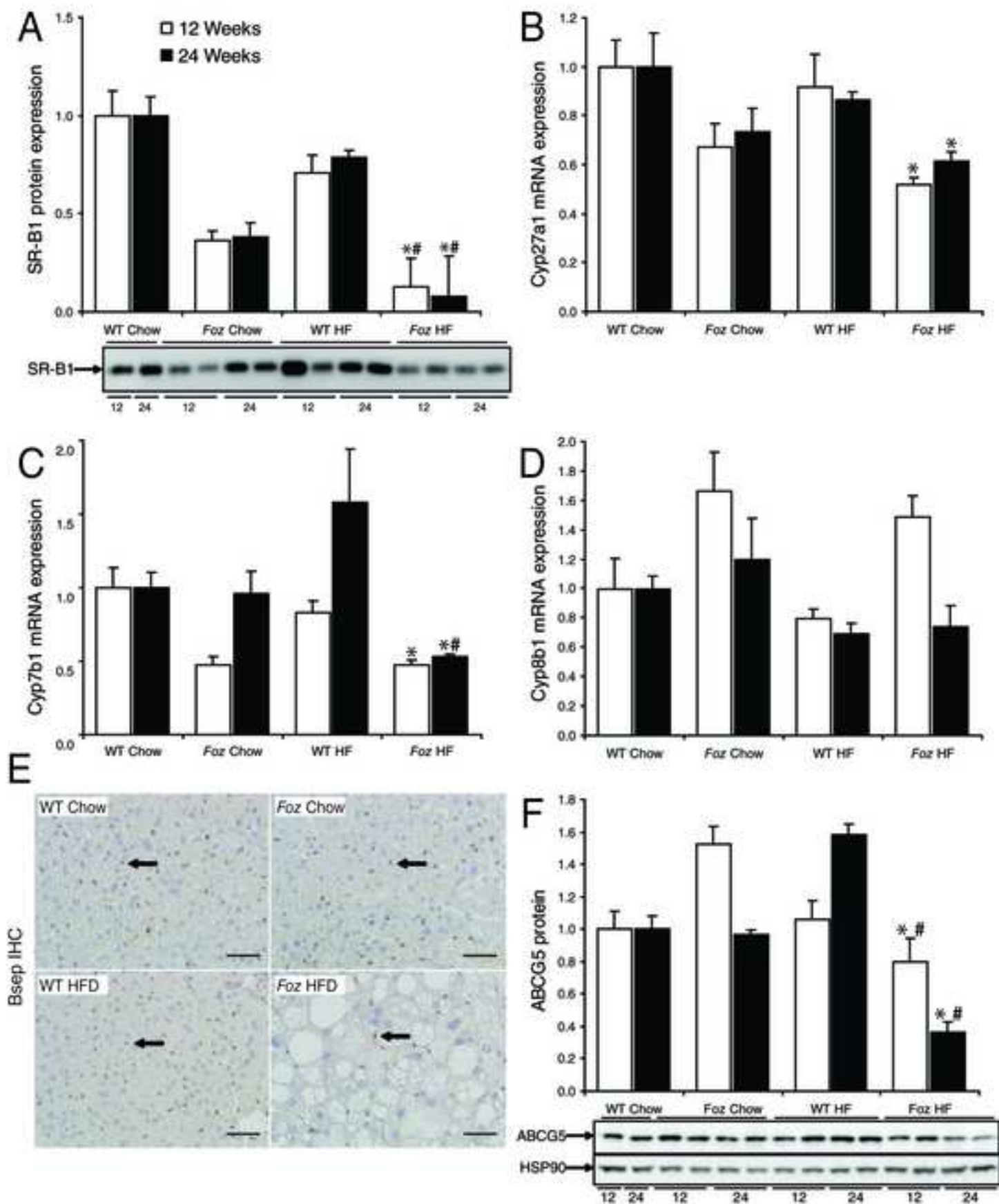
Gene	Sense	Anti-sense
CEH	ACGCTTGCCAGACCCTCTTC	CTCAGCCACTTCAGCATCGC
Cyp27a1	TCATCGCACAAAGGAGAGCAATG	CGTTTAAGGCATCCGTGTAGAGC
Cyp7a1	TTGTTCAAGACCGCACATAAAGCC	CGTAGACGGATCAGTTCAGAGACC
Cyp7b1	TTTCAGTCCACTTCACCAGAGAAC	GCACAGCCTCAGAACCTCAAGA
Cyp8b1	CCCTGAGCCCACAGCCTTC	GGATCTTCTTGCCCCACTTGTAG
FXR	TGCGATTACCACCACCACCTG	CCGAACCTTAGCCAGCCACCA
LRH-1	GGCTCCGTTCCCTTCAGTTTCG	TTCACCTGCTCTTGGACACCTTC
Shp	AAGGGCACGATCCTCTTCAACC	CAGGGCTCCAAGACTTCACACA

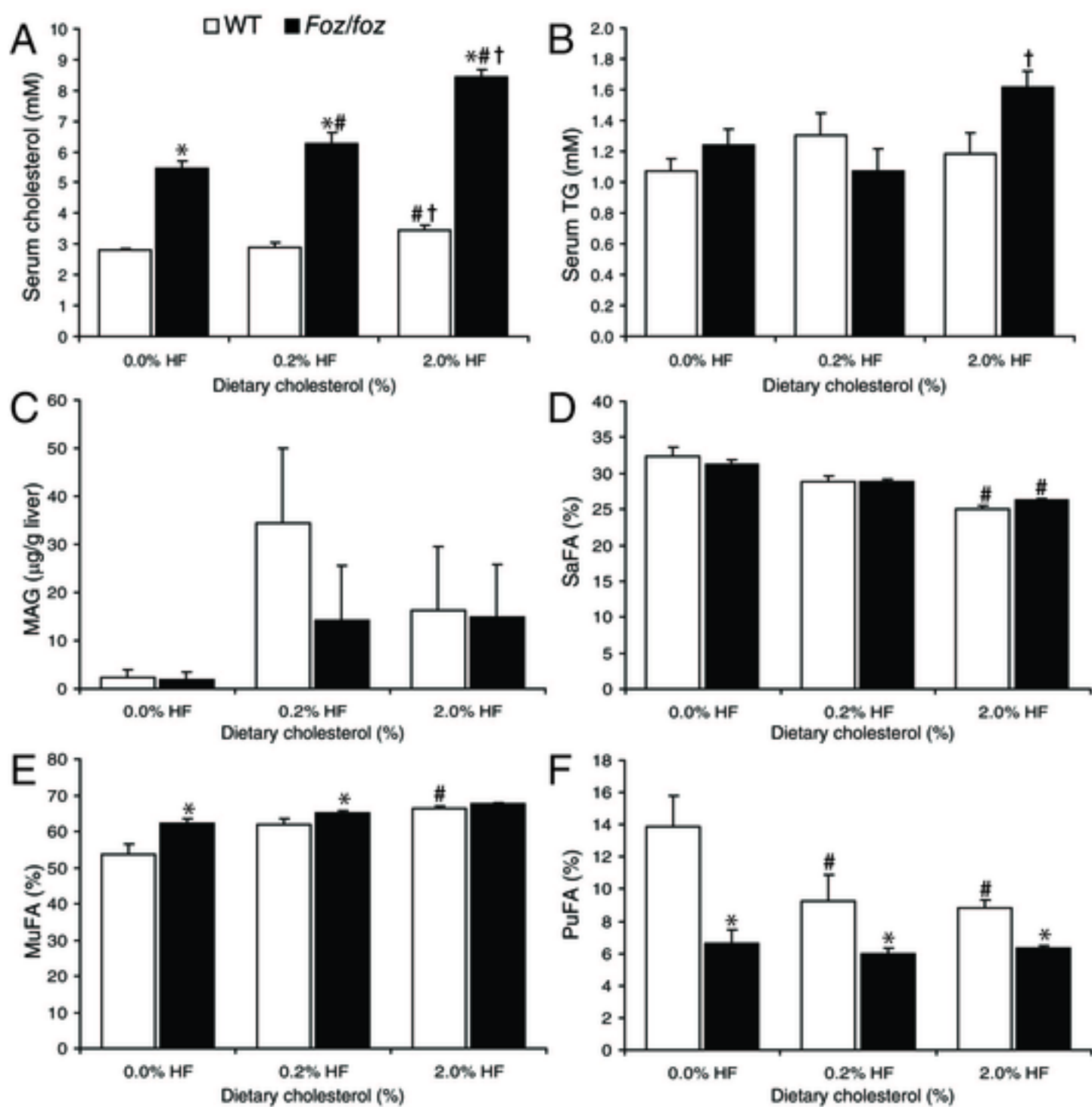
Abbreviations: CEH, cholesteryl ester hydrolase; Cyp27a1, sterol 27-hydroxylase; Cyp7a1, 7- α -hydroxylase; Cyp7b1, oxysterol 7- α -hydroxylase; Cyp8b1, sterol 12- α -hydroxylase; FXR, farnesoid X receptor; LRH-1, liver-receptor homolog-1; Shp, small heterodimer partner

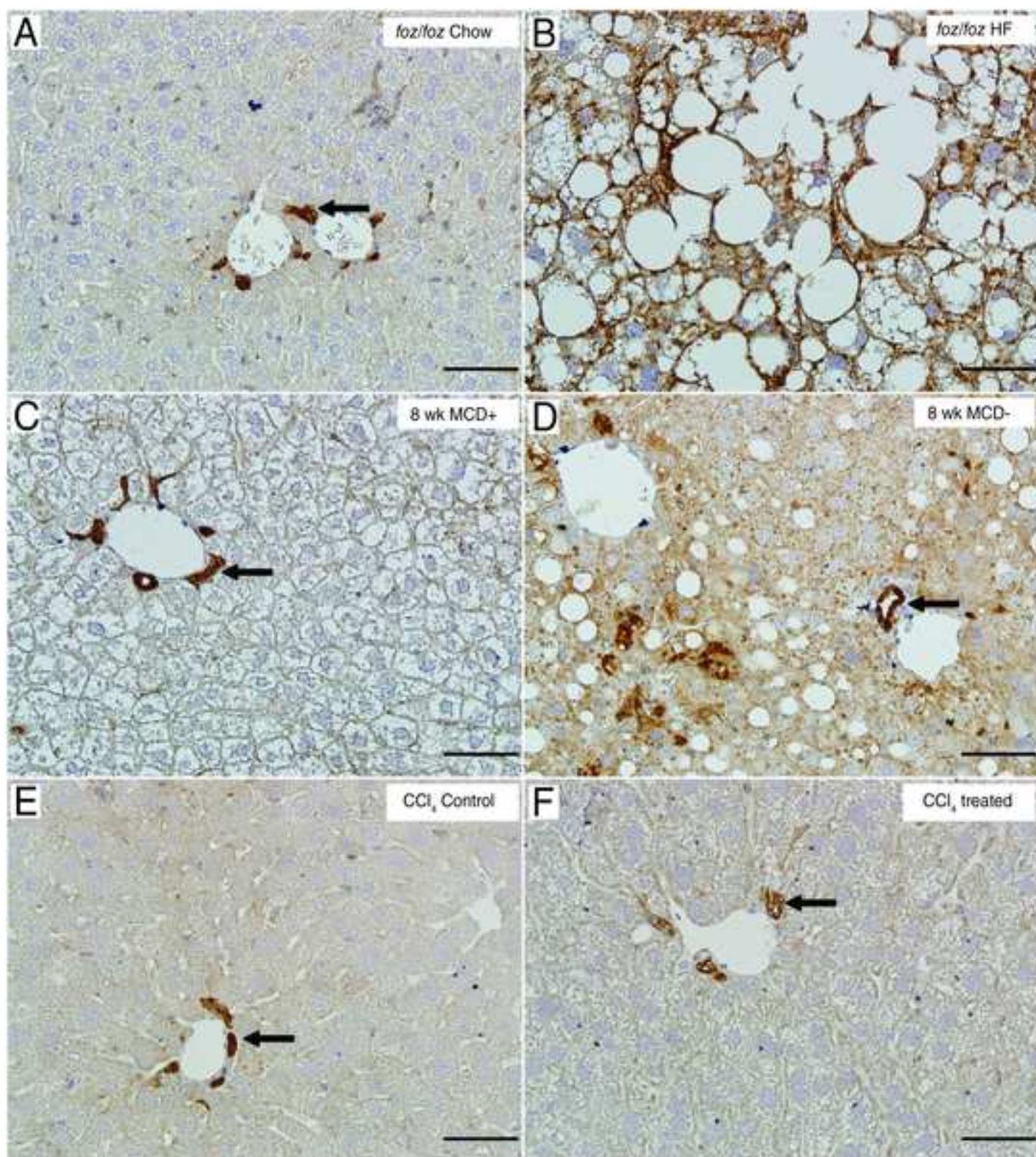
Supplementary Table 2. Antibody details and conditions used for western blotting (WB) and immunohistochemistry (IHC).

Antibody	Supplier	Catalog #	Application	Dilution
α -ABCG5	Santa Cruz	sc-25796	WB	1:500
α -ABCG8	Santa Cruz	sc-30111	WB	1:350
α -ACAT2	Cayman Chemicals	100027	WB	1:180
α -Bsep	Santa Cruz	sc-74500	WB	1:180
α -Bsep	Santa Cruz	sc-25571	IHC	1:200
α -F4/80	AbD Serotec	MCA497R	IHC	1:150
α -FXR	Abcam	ab28480	WB	1:500
α -HSP90	R&D systems	AF3775	WB	1:2000
α -LDLR	Abcam	ab52818	WB, IHC	1:1800, 1;200
α -LRH-1	Abcam	ab41901	WB	1:500
α -Shp	Santa Cruz	sc-23057	WB	1:200
α -SR-B1	Abcam	ab52629	WB, IHC	1:1800, 1:200
α -SREBP-2	Abcam	ab28482	WB	1:500

Abbreviations: ABC, ATP-binding cassette protein; ACAT, acyl-CoA:cholesterol acyltransferase; Bsep, bile salt exporter protein; FXR, farnesoid X receptor; LDLR, LDL-receptor; LRH-1, liver receptor homolog-1; Shp, small heterodimer partner; SR-B1, scavenger receptor B-1; SREBP-2, sterol response element binding protein-2. Antibodies were purchased from Abcam (Cambridge, UK), AbD Serotec (Oxford, UK), Cayman Chemicals (Ann Arbor, MI, USA), R&D Systems (Minneapolis, MN, USA), and Santa Cruz Biotechnology, Inc (Santa Cruz, CA. USA).







Supplementary Figure 1. Differentially regulated pathways involved in cholesterol homeostasis.

In addition to the pathways illustrated in Figure 2, we studied: (A) Scavenger receptor-B1 (SR-B1) protein expression, and (B) *Cyp27a1*, (C) *Cyp7b1*, (D) *Cyp8b1* mRNA expression at 12- (□) and 24- (■) weeks in WT and *foz/foz* mice (*n* values as per METHODS). (E) Bile salt exporter protein (Bsep) IHC staining in 24-week WT and *foz/foz* mouse livers produced similar results to WB analyses (Figure 2). (F) ATP-binding cassette-G5 (ABCG5) protein expression in mice at 12- and 24- weeks. Scale bars represent 50 μm. Arrows indicate positive staining. **P*<0.05, vs. diet-matched control. #*P*<0.05, vs. genotype-matched, 0.2% cholesterol groups. †*P*<0.05, vs. genotype-matched, 2.0% cholesterol groups.

Supplementary Figure 2. Dietary cholesterol increases serum cholesterol, but fails to alter other lipid profiles in HF-fed WT and *foz/foz* mice.

(A) Total serum cholesterol and (B) triglyceride (TG) levels in WT (□) and *foz/foz* (■) mice (*n* values as per METHODS) fed HF-diet containing 0, 0.2 or 2.0% (w/w) cholesterol for 24-weeks. (C) Monoacylglycerides (MAG), (D) saturated FFAs (SaFA), (E) mono-unsaturated FFAs (MuFA), and (F) poly-unsaturated FFAs (PuFA) were determined by HPLC. **P*<0.05, vs. diet-matched control. #*P*<0.05, vs. genotype-matched, 0.0% cholesterol groups. †*P*<0.05, vs. genotype-matched, 0.2% cholesterol groups.

Supplementary Figure 3. Comparison between LDLR localization in *foz/foz*, methionine and choline-deficient (MCD) and carbon tetrachloride-treated mice .

LDLR localization in (A) chow- and (B) HF-fed *foz/foz* mice at 24 weeks, (C) MCD control and (D) MCD-deficient mice at 8 weeks, and (E) carbon tetrachloride- (CCl₄) control and (F) – treated mice at 4 weeks. Scale bars represent 20 μm.