

Supplemental Information

Kit Name	Manufacturer	Catalog #	Manufacturer Protocol #
Total Bile Acid (TBA) Enzymatic Cycling Kit Assay	Bioquant	BQ 042A-EALD	1435702385
Liquid ALT (SGPT) Reagent Set	Pointe Scientific	A7526	P803-A7526-01 Rev. 12/09
Alkaline Phosphatase (Liquid) Reagent Set	Pointe Scientific	A7516	P803-A7516-01 Rev. 11/11
Cholesterol (Liquid) Reagent Set	Pointe Scientific	C7510	P803-C7510-01 Rev. 11/11
Triglyceride (GPO)(Liquid) Reagent Set	Pointe Scientific	T7532	P803-T7532-01 Rev. 12/09
TriZOL Reagent	Thermo Fisher Sci.	15596018	MAN00001271 Rev. A

Oral Glucose Tolerance Test:

Mice were fasted overnight and then given an oral gavage of 20% glucose solution (10 uL/g bodyweight; 2 mg glucose/gram body weight). A drop of blood was collected from the tail 0, 15, 30, 60 and 120 minutes post gavage. Blood was immediately analyzed using a glucometer to measure blood glucose levels.

Oil Red O Stain:

Frozen livers were sectioned at 8 microns and fixed in formalin. Oil Red O working solution was created by diluting 30 mL of stock stain (0.5% Oil Red O in isopropanol) in 20 mL of mH₂O. Slides were rinsed with 60% isopropanol and stained with freshly prepared Oil Red O working solution for 15 minutes. Slides were rinsed with 60% isopropanol and then counterstained with hematoxylin.

Immunohistochemistry staining of Desmin:

Liver sections were deparaffinized in xylene and rehydrated. Antigen retrieval was performed using 10 mM citrate buffer for 10 minutes. Endogenous peroxidase activity was quenched using 3% H₂O₂ for 15 minutes. Sections were blocked with 10% normal rabbit serum in PBS for 2.5 hours at room temperature. Sections were incubated with 1:100 goat anti-desmin (PIPA519063; Thermo Fisher Scientific, Waltham, MA) primary antibody in 5% rabbit serum overnight at 4°C. Slides were incubated with anti-goat secondary for 30 minutes and then ABC reagent for 30 minutes (Vectastain Kit; Vector Laboratories, Burlingame, CA). Slides were then stained with DAB. Nuclei were counterstained with hematoxylin. Slides were dehydrated and mounted.

Supplemental Table 1: NAFLD Activity Scores. Data presented as average score (SD).

	Lipid Accumulation	Hepatocyte Ballooning and Necrosis	Inflammation	Overall
WT Chow	0.25 (0.5)	0 (0)	0 (0)	0.25 (0.5)
WT HFD	2.8 (0.4)	0.8 (0.4)	0.4 (0.5)	4 (1.2)
Fgf15^{-/-} Chow	0.25 (0.5)	0 (0)	0.25 (0.5)	0.5 (0.6)
Fgf15^{-/-} HFD	2.75 (0.5)	0.5 (0.6)	1 (0.8)	4.25 (1.8)