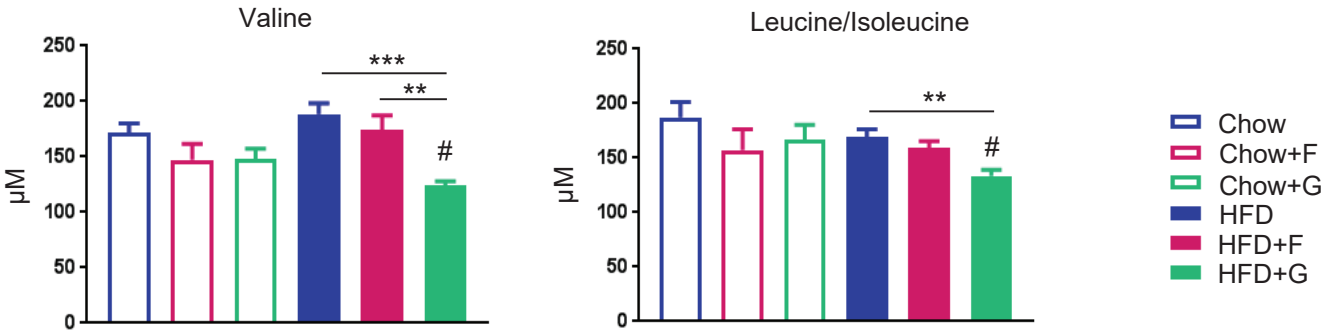
Supplemental figures

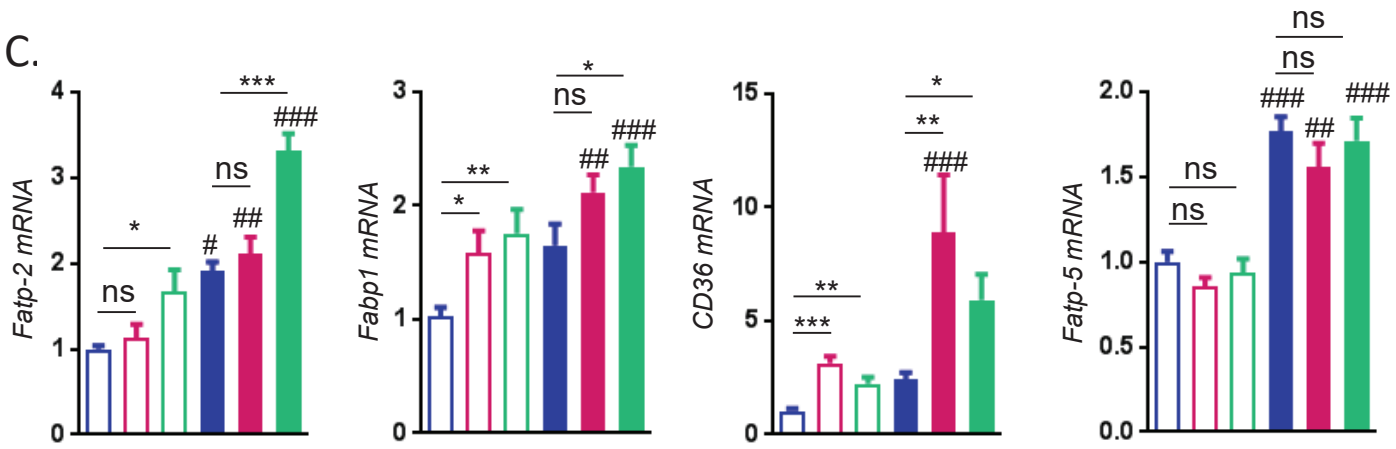
A.

	Chow	Chow+F	Chow+G	HFD	HFD+F	HFD+G
Weight (g)	28.9 ±1.4	36.5 ±0.6	37.7 ±1.0	41.2 ±1.6	45.9 ±0.6	40.6 ±1.3
Glucose (mg/dl)	135 ±10	151 10	134 9	186 ±6	202 ±9	143 ±11
Insulin (ng/ml)	0.6 ±0.1	0.8 ±0.2	0.4 ±0.1	1.0 ±0.1	1.1 ±0.1	0.5 ±0.1
Liver wt (g)	1.3 ±0.2	1.6 ±0.1	1.2 ±0.1	1.4 ±0.1	2.0 ±0.1	1.7 ±0.1
Food intake (kcal)	10.7 ±0.6	11.7 ±1.2	11.6 ±1.7	14.8 ±0.8	13.5 ±0.7	11.0 ±1.4
Water intake (kcal)	0	6.9 ±0.4	9.1 ±0.5	0	5.1 ±0.4	8.5 ±0.3
Total kcal intake	10.7 ±0.6	18.6 ±1.5	20.7 ±2.0	14.8 ±0.8	18.6 ±0.7	19.4 ±1.4
Steat	-	↑	↑	↑↑	↑↑	↑↑
Fatty acid Synthesis	-	↑↑↑	↑	-	↑↑	-
Srebp1	-	↑↑↑	↓	↓	↑↑	↓
Chrebp	-	-	↑↑↑	↓	↑	↑↑↑

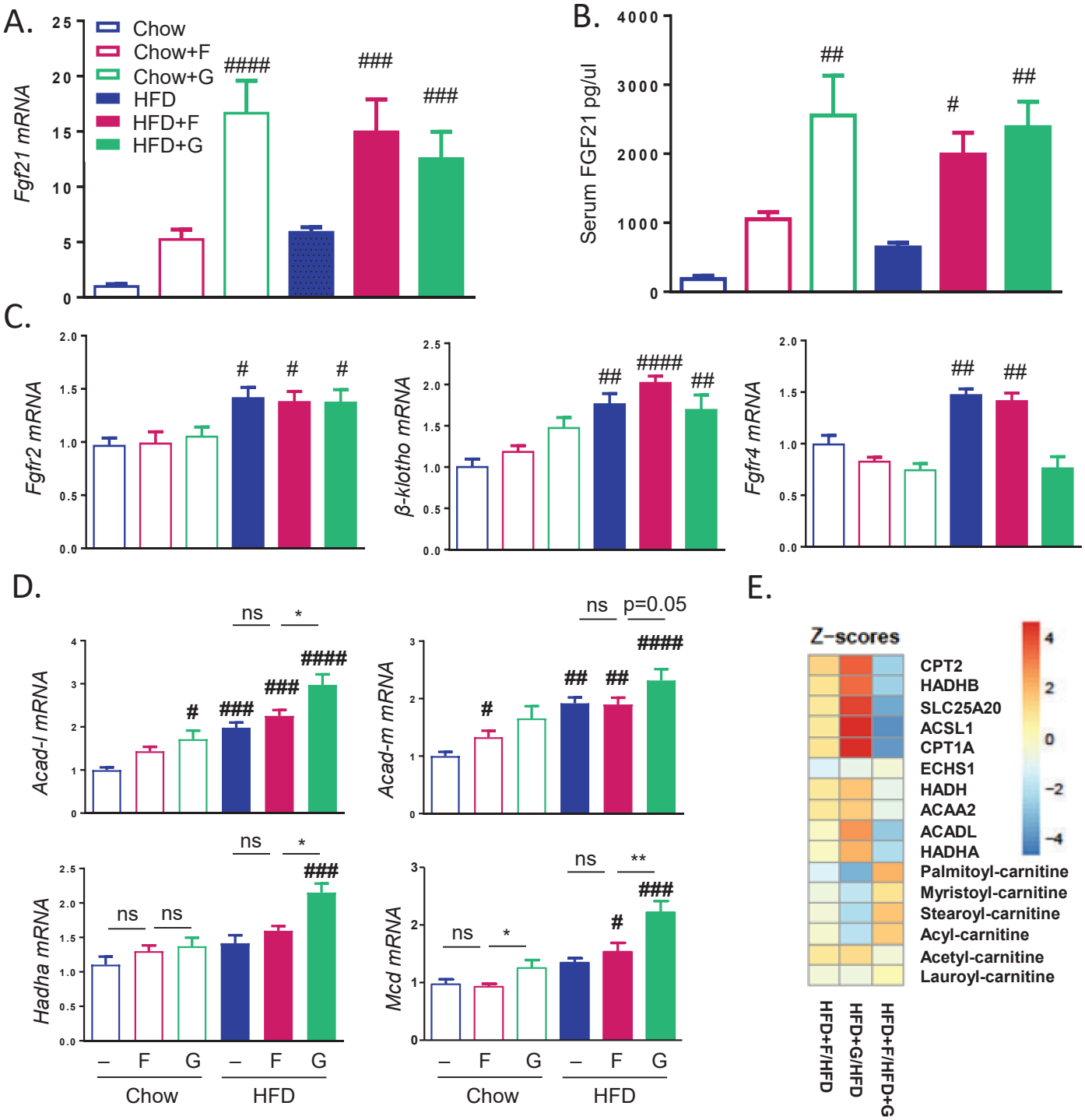
B.



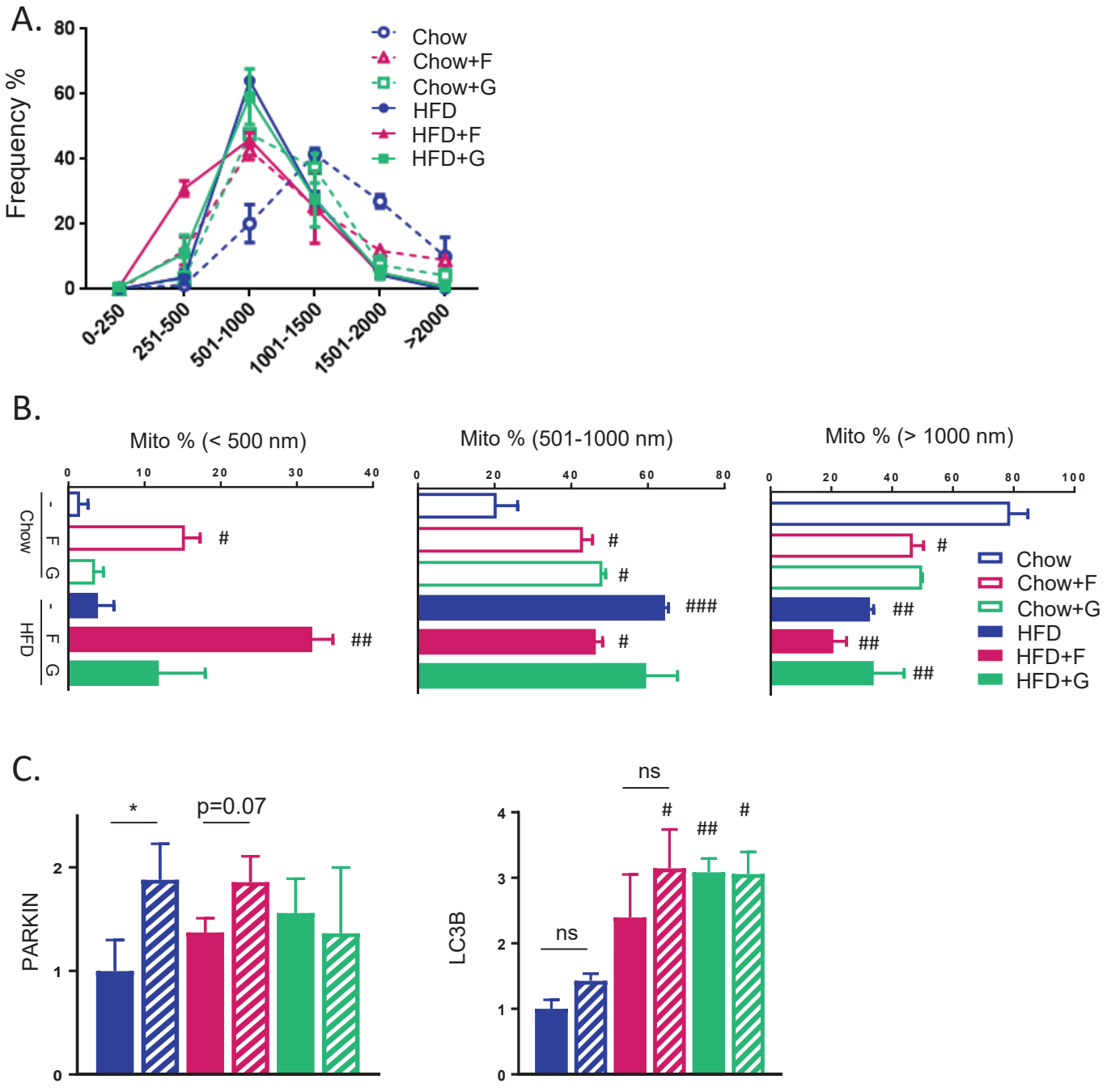
C.



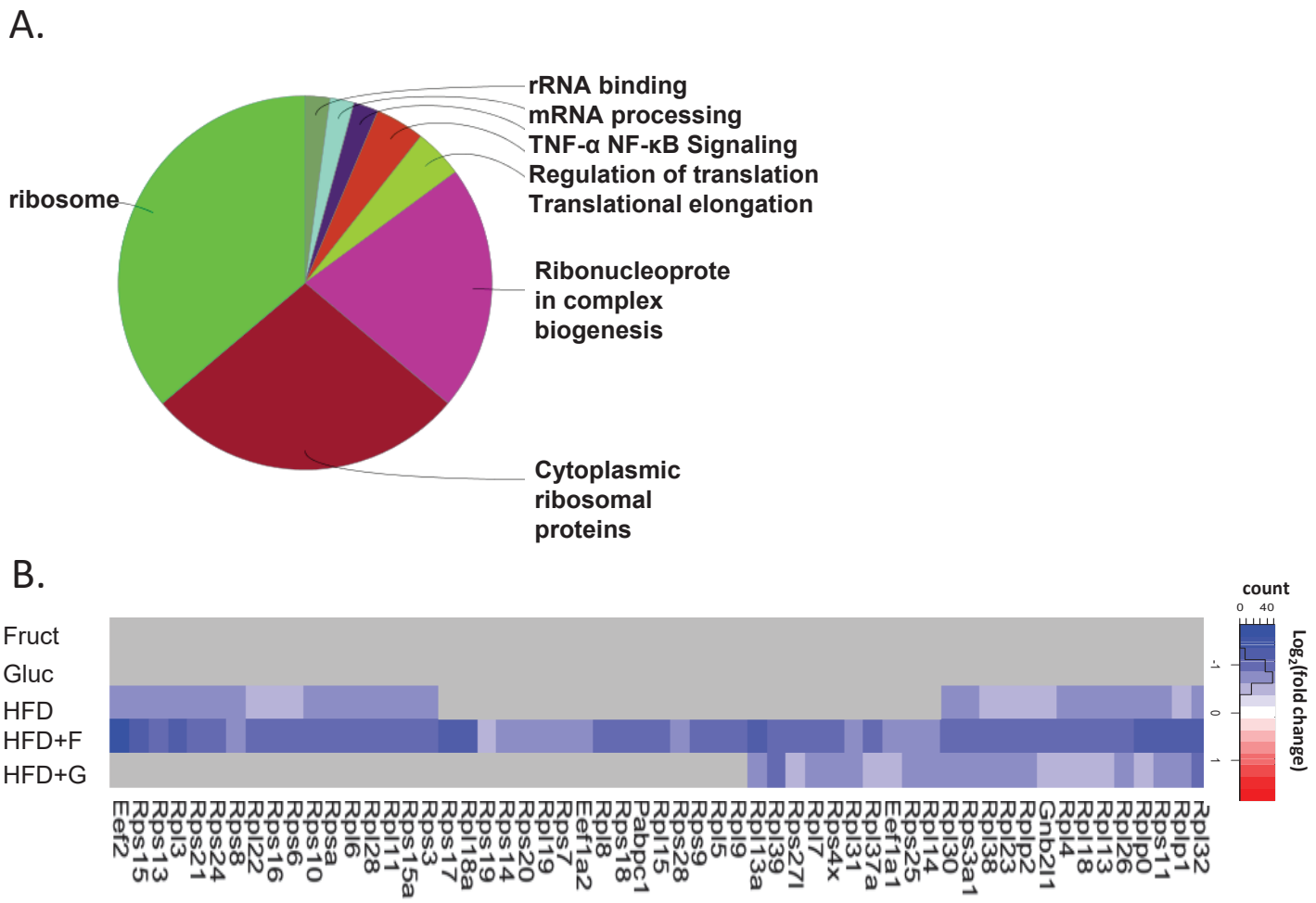
Sup. Fig. 1: Summary of metabolic phenotype in mice exposed to different diets. Related to figure 1.
A) Summary of metabolic phenotype in mice exposed to different diets for 10 weeks as published in Softic, JCI. 2017. B) Serum branched chain amino acid levels in the same mice. n = 6 mice per group. C) Liver mRNA expression of enzymes regulating fatty acid transport in mice after 10 weeks on the diets. n=7-8 mice per group. The data represent mean ±SEM. Significant difference between diet types as compared to the Chow group is noted with a number sign (#) and significant difference within the diet groups is designed by a star (*).



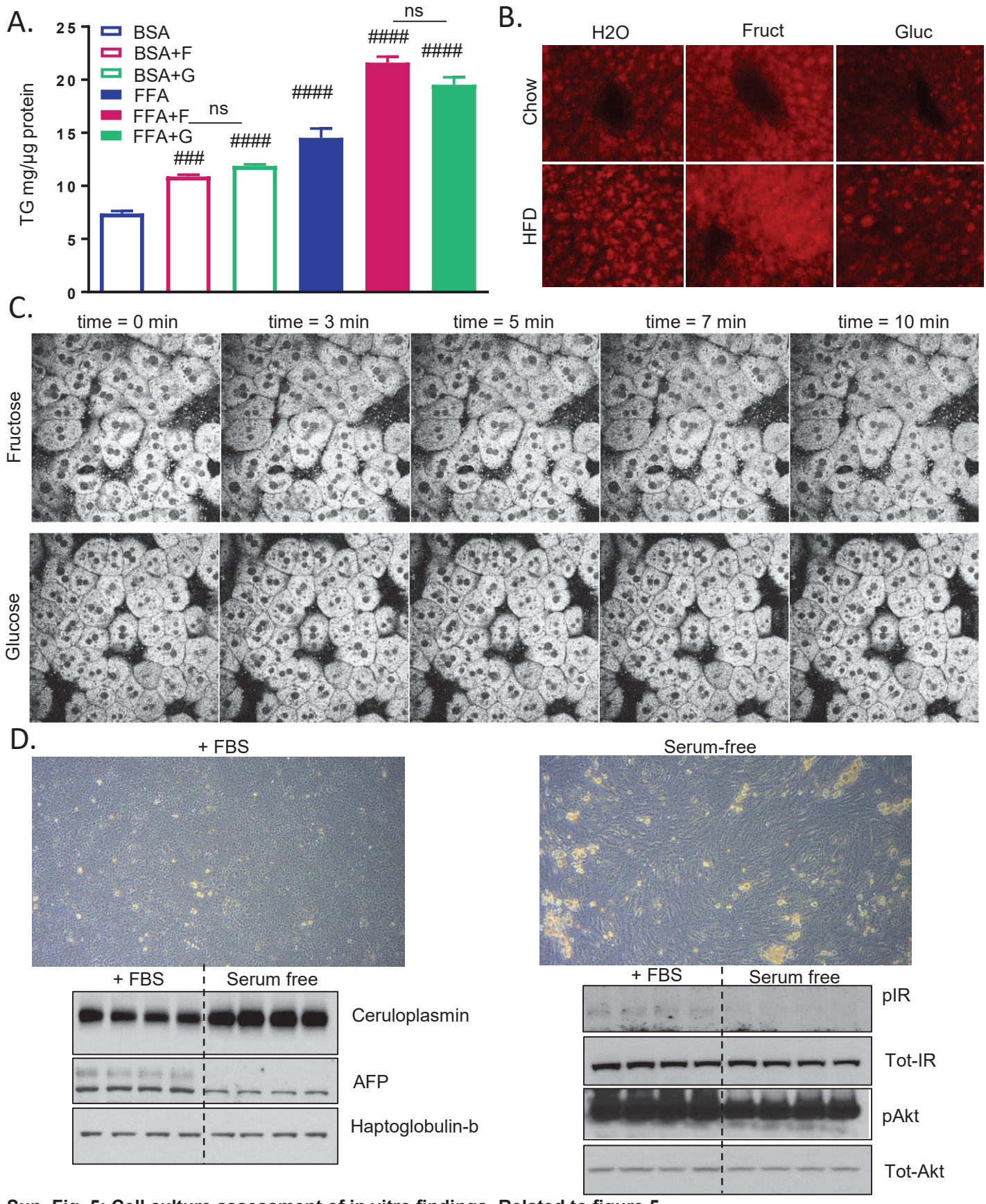
Sup. Fig. 2: Hepatic gene expression and limited serum and hepatic metabolites. Related to figure 2.
A) Hepatic *Fgf21* expression and B) serum FGF21 levels from mice after 10 weeks on respective diets. The data are represented as mean ± SEM, n = 8 mice per group. C) Expression of Fgf receptors and co-receptors in the liver. D) Liver mRNA expression of enzymes regulating fatty acid oxidation in the livers of mice after 10 weeks on diets. n=7-8 mice per group. The data represent mean ±SEM. Significant difference between diet types as compared to the Chow group is noted with a number sign (#) and significant difference within the diet groups is designed by a star (*).E) heat map of combined RNAseq and hepatic metabolome data showing mitochondrial beta-oxidation of long chain saturated fatty acids pathway.



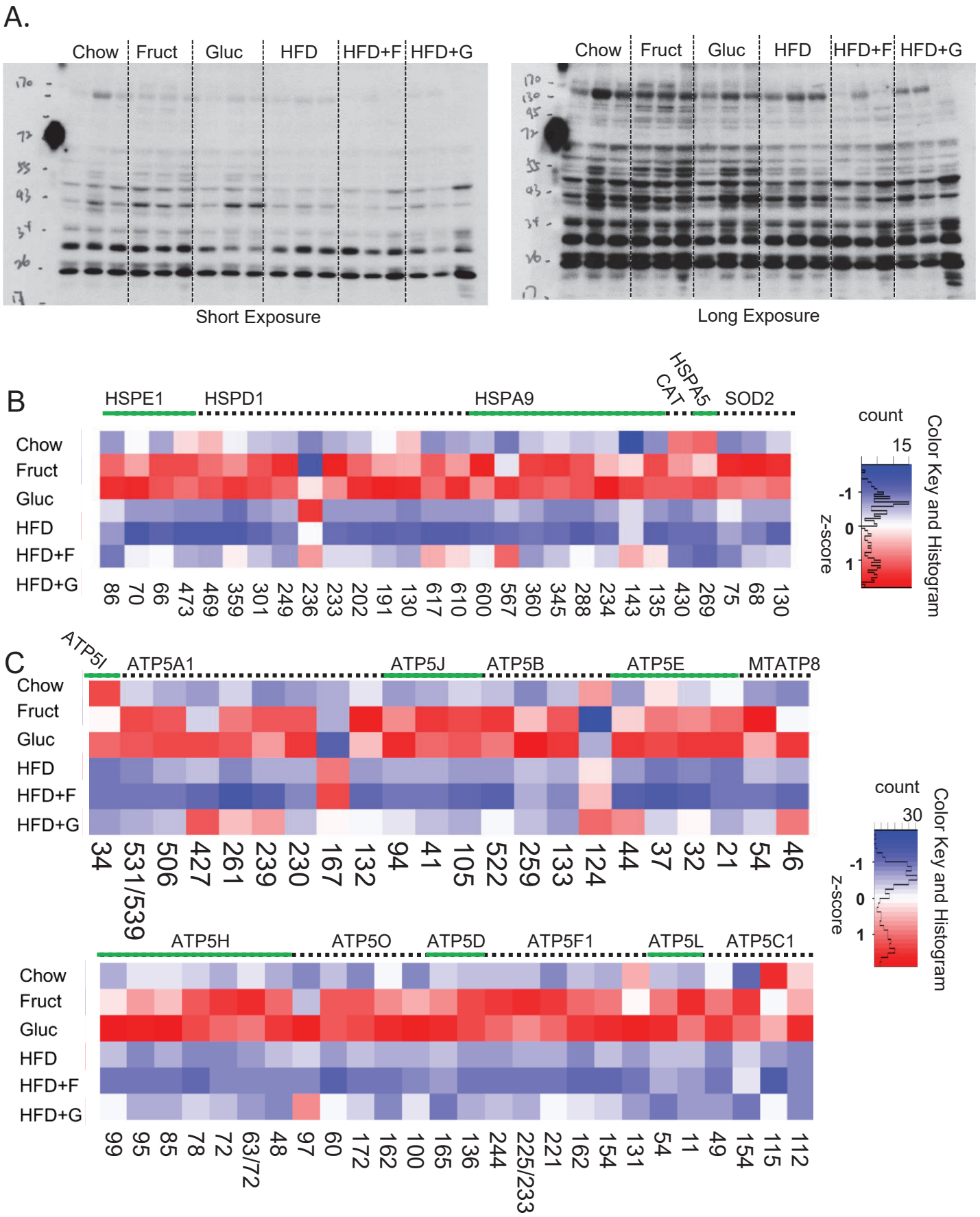
Sup. Fig. 3: Mitochondrial size and western blot quantification. Related to figure 3.
A) Histogram of mitochondrial size as measured using image J software utilizing electron microscopy images from the livers of mice after 10 weeks on diet. n=5 per group. B) Percent of small, medium and large mitochondrial from these mice. The data represent mean ±SEM. # indicates significant difference as compared to chow group. C) Image J quantification of western blots shown in figure 3G of proteins involved in mitophagy pathway. n=3 mice per group.



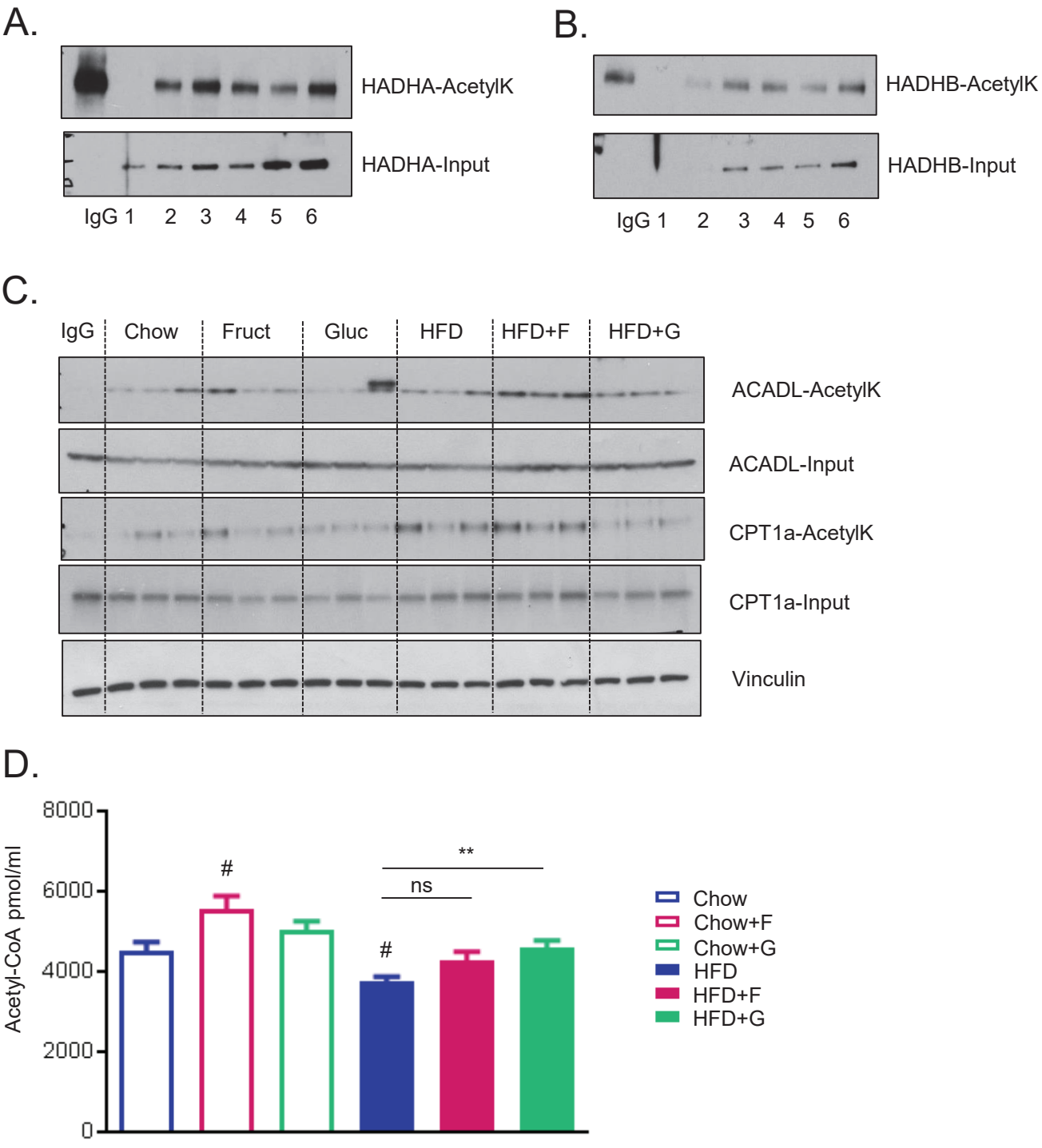
Sup. Fig. 4: Proteomic quantification of ribosomal proteins. Related to figure 4.
A) Pie-chart analysis of ribosomal proteins quantified by Nano-liquid chromatography – tandem mass spectrometry from isolated mitochondrial fraction from the livers of mice after 10 weeks on the diets. B) Heat map analysis of ribosomal proteins from the same mice. n = 5 mice per each diet and 1 mitochondrial prep per mouse.



Sup. Fig. 5: Cell culture assessment of in vitro findings. Related to figure 5.
A) Triglyceride levels in AML-12 hepatocytes 48 hours after treatment with fructose or glucose with or without addition of free fatty acid s. n = 6 wells per group. The data represent mean ±SEM. B) DHE fluorescence in the livers of mice after 10 weeks on respective diets. C) NAD(P)H autofluorescence as measured by multiphoton microscopy in isolated primary hepatocytes, treated with 25 mM fructose or glucose for 10 min. D) Morphology of AML-12 cells grown in full and serum free media for 7 days. Western blots of hepatocyte markers and insulin signaling in these cells.



Sup. Fig. 6: Acetylation profile of selected proteins and whole liver lysates. Related to figure 6.
A) Western blot analysis from whole liver lysates obtained from mice after 10 weeks on the diets. n = 3 mice per group. Short and long exposures are shown. Heat map analysis of mitochondrial proteins involved in B) ROS and C) ATP production pathways, from the same mice. n = 5 mice per each diet.



Sup. Fig. 7: Immunoprecipitation and western blot of acetylated proteins. Related to figure 7. Western blot analysis for acetylated A) HADHA and B) HADHB determined by immunoprecipitation with anti-HADHA/B antibody followed by western blot analysis with anti acetyl-lysine antibody. Numbers represent 3 pooled samples from each group where 1= Chow, 2= Chow+F, 3= Chow+G, 4= HFD, 5= HFD+F, 6= HFD+G group C) Western blot analysis of acetylated and total ACADL and CPT1a determined by immunoprecipitation with anti-acetyl-lysine antibody, followed by western blot analysis with anti-ACADL and anti-CPT1a antibody. D) Liver acetyl-CoA levels were measured using targeted mass spectrometry in mice after10 weeks on diets. Data represent mean ±SEM. n = 6 mice per group