Table S1. Serum biochemical parameters

	n	Glucose (mg/dL)	Creatinine (mg/dL)	Bilirubin (mg/dL)	AST (IU/L)	ALT (IU/L)	CK (IU/L)	AP (IU/L)	Cholesterol (mg/dL)	LDL (mg/dL)	HDL (mg/dL)	TGL (mg/dL)	Albumin (g/dL)
CD-Veh	7	128,83 ± 6,80	0,51 ± 0,06	0,11 ± 0,01	160,33 ± 21,21	34,71 ± 3,08	827 ± 103,94	120,43 ± 6,05	89,57 ± 8,11	29,57 ± 3,18	54,00 ± 5,17	28,5 ± 2,17	2,99 ± 0,07
HFGFD-Veh	6	151,67 ± 14,91	0,50 ± 0,03	0,12 ± 0,02	168,17 ± 20,08	73,00 ± 16,63***	751,17 ± 85,97	131,83 ± 8,56	79,83 ± 5,72	27,33 ± 2,93	47,67 ± 3,56	24,17 ± 2,7	2,95 ± 0,07
HFGFD-At	8	152,50 ± 16,26	0,66 ± 0,03*#	0,12 ± 0,02	128,88 ± 10,82	37,00 ± 2,73###	787,86 ± 97,28	130,00 ± 13,13	76,13 ± 3,45	25,25 ± 1,83	45,38 ± 2,78	27,25 ± 4,55	2,95 ± 0,08
HFGFD-Am^{hi}	7	152,57 ± 17,05	0,54 ± 0,04	0,11 ± 0,01	131,5 ± 9,48	42,71 ± 3,48##	882,83 ± 72,75	148,86 ± 10,02	79,43 ± 8,75	24,57 ± 2,64	47,71 ± 6,92	36,14 ± 3,92	3,06 ± 0,06
HFGFD-AtAm^{hi}	8	141,5 ± 10,65	0,57 ± 0,04	0,10 ± 0,02	127,88 ± 10,14	34,25 ± 2,47###	723,14 ± 105,17	139,00 ± 8,93	72,75 ± 5,85*	23,88 ± 2	42,13 ± 4,21	33,75 ± 4,6	2,90 ± 0,06
HFGFD-Am^{lo}	7	146,86 ± 17,95	0,59 ± 0,06	0,12 ± 0,01	171,29 ± 19,54	38,43 ± 3,67###	857,00 ± 123,09	127,86 ± 14,35	77,71 ± 3,56	24,14 ± 2,05	46,29 ± 2,83	36,57 ± 5,42	2,97 ± 0,03
HFGFD-AtAm^{lo}	8	133,13 ± 13,35	0,50 ± 0,03	0,14 ± 0,01	135,13 ± 18,10	39,75 ± 4,75###	797,63 ± 149,32	138,00 ± 12,97	73,75 ± 3,07*	23,50 ± 1,97	45,38 ± 2,06	23,75 ± 4,04	2,96 ± 0,05

Values are expressed as mean ± SEM. n, number of rats; AST, aspartate aminotransferase; ALT, alanine aminotransferase; CK, creatine kinase AP, alkaline phosphatase; TGL, triglycerides. CD (control diet); HFGFD-Veh (vehicle); HFGFD-At (10 mg/kg/day atorvastatin); HFGFD-Am^{hi} (30 mg/kg/day ambrisentan); HFGFD-AtAm^{hi} (10 mg/kg/day atorvastatin and 30mg/kg/day ambrisentan); HFGFD-Am^{lo} (2 mg/kg/day ambrisentan); HFGFD-AtAm^{lo} (10mg/kg/day atorvastatin and 2mg/kg/day ambrisentan). *p <0.05, vs. CD; #p <0.05 vs. HFGFD-Veh (ANOVA).

Table S2. *NASH Clinical Research Network Scoring System Definitions (Kleiner et al., 2005)*

Item	Definition	Score
Steatosis	Low-to-medium power evaluation of parenchymal involvement by steatosis	
	<5%	0
	5-33%	1
	33-66%	2
	>66%	3
Lobular inflammation	Overall assessment of all inflammatory foci	
	No foci	0
	<2 foci per 200 x field	1
	2-4 foci per 200 x field	2
	>4 foci per 200 x field	3
Hepatocellular ballooning	None	0
	Few balloon cells	1
	Many cells/prominent ballooning	2

Table S3. Primary antibodies for Western blot.

Antibody	Company	Reference	Dilution
Rabbit polyclonal anti-P-eNOS (Ser1177)	Cell Signaling	#9571	1:250
Mouse monoclonal anti-eNOS	BD transduction Labs.	610296	1:500
Rabbit polyclonal anti-P-Akt (Ser473)	Cell Signaling	#9271S	1:500
Rabbit polyclonal anti-Akt	Cell Signaling	#9272S	1:500
Goat polyclonal anti-KLF2	Santa Cruz biotechnology	Sc-18690	1:200
Mouse monoclonal anti-ET-1	Abcam	Ab2786	1:250
Mouse monoclonal anti-GAPDH	Thermo Fisher Scientific	Am4300	1:5000

Phosphorylated endothelial nitric oxide synthase (P-eNOS), phosphorylated protein kinase B (P-Akt,), Kruppel-like factor 2 (KLF2), endothelin-1 (ET-1), and glyceraldehyde-3-phosphate dehydrogenase (GAPDH).

Table. S4. Primers used in qPCR.

Gene symbol	Gene name	Gene alias	Assay ID
Acta2	Actin, alpha 2, smooth muscle, aorta	αSMA	Rn01759928
Col1a1	Collagen, type I, alpha 1	COL1A1	Rn01463848
Des	Desmin		Rn00574732
Edn1	Endothelin 1	Et1	Rn00561129
Ednra	Endothelin receptor type A	ETRA, ET_A	Rn00561137
Ednrb	Endothelin receptor type B	ETRB, ET_B	Rn00569139
Mmp2	Matrix metallopeptidase 2		Rn01538170
Pdgfrb	Platelet derived growth factor receptor, beta polypeptide	PDGFRβ	Rn00709573

All probes are from Thermo Fisher Scientific.
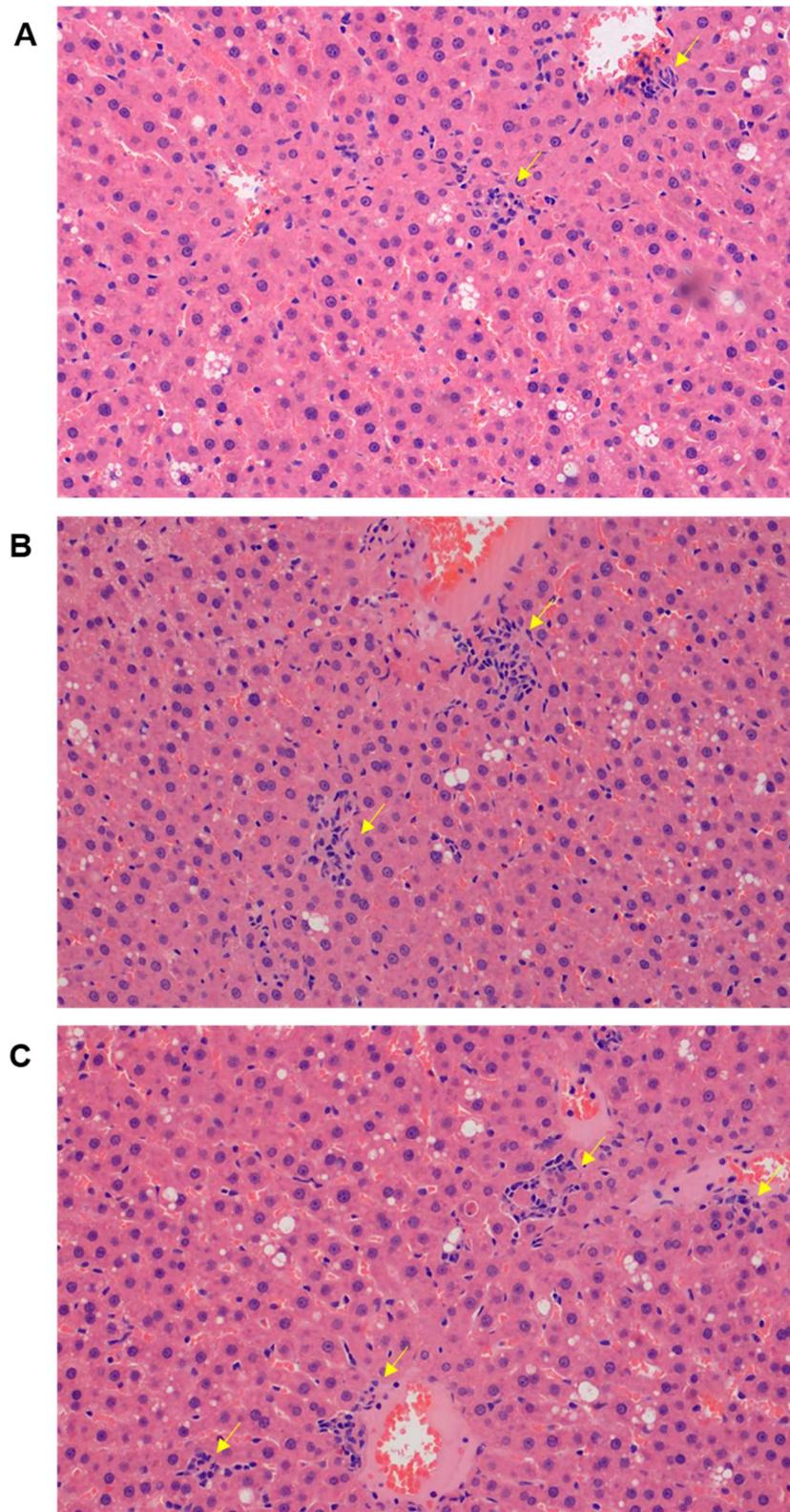
Figure S1. Representative images of lobular inflammation in HFGFD fed individuals. Images correspond to liver sections (20x magnification) stained with hematoxylin-eosin used to perform the histological evaluation. Yellow arrows point inflammatory foci.
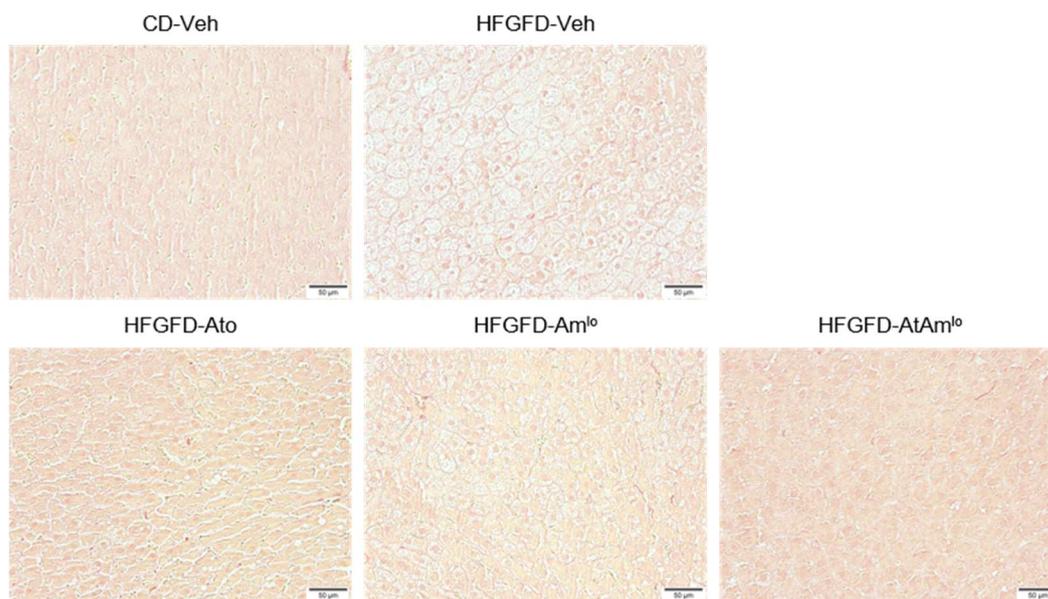
Figure S2. Representative images (20x magnification) of liver sections stained with Sirius Red to asses fibrosis.
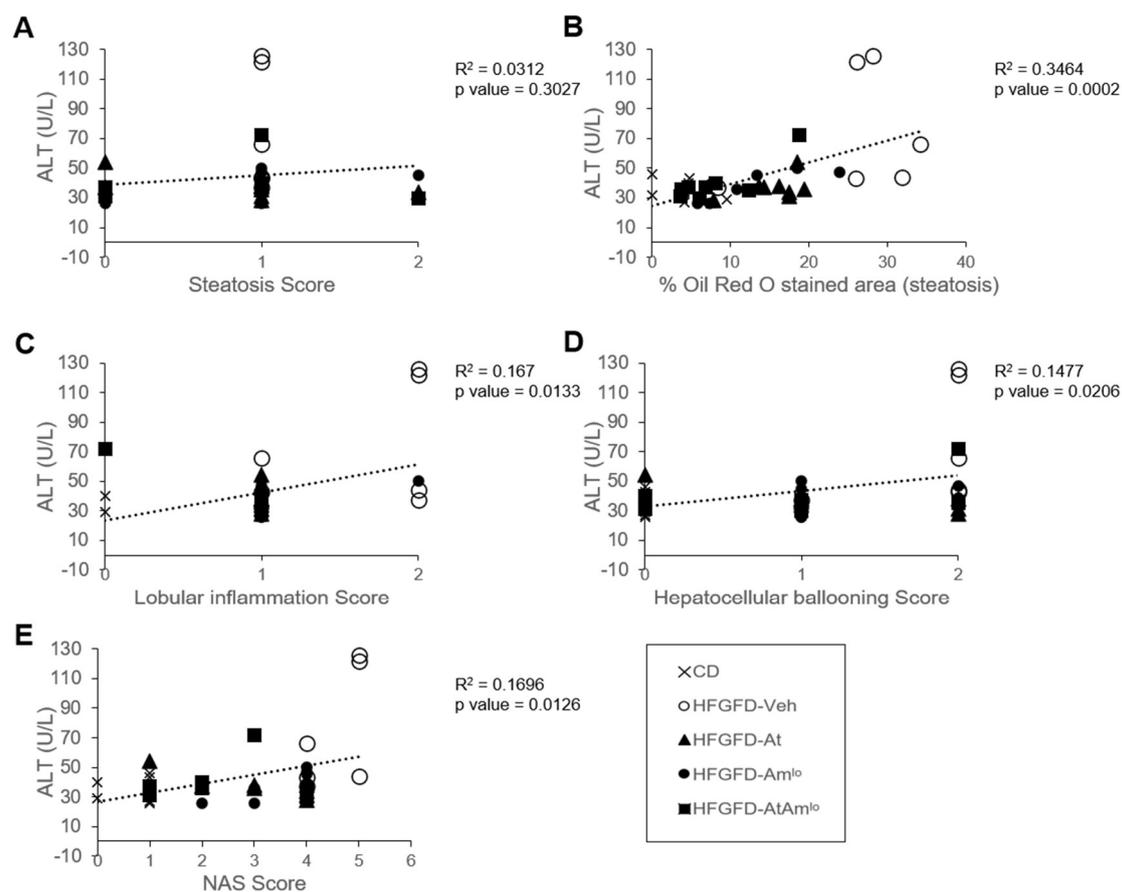
Figure S3. Correlations between serum ALT levels and (A) steatosis score (B) Oil Red O stained % area (C) lobular inflammation score (D) hepatocellular ballooning score and (E) NAFLD activity score (NAS).
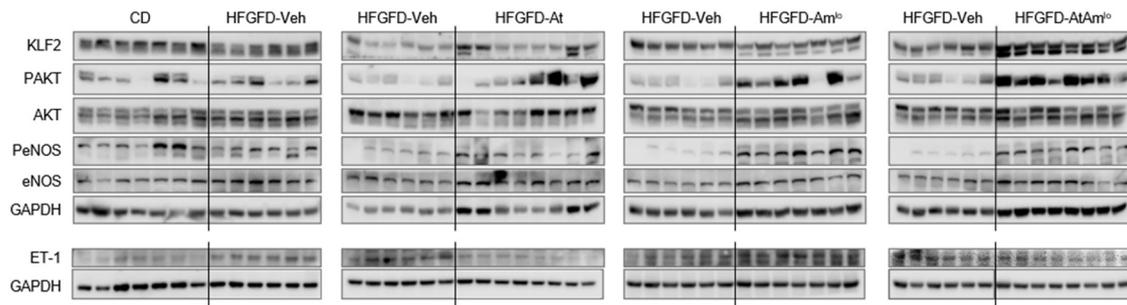
Figure S4. Complete Western blot images of P-Akt, phosphorylated protein kinase B, P-eNOS, phosphorylated endothelial nitric oxide synthase, KLF2, Kruppel-like factor 2; ET-1, endothelin-1; and GAPDH, glyceraldehydes 3-phosphate dehydrogenase from liver samples.