Figure S1

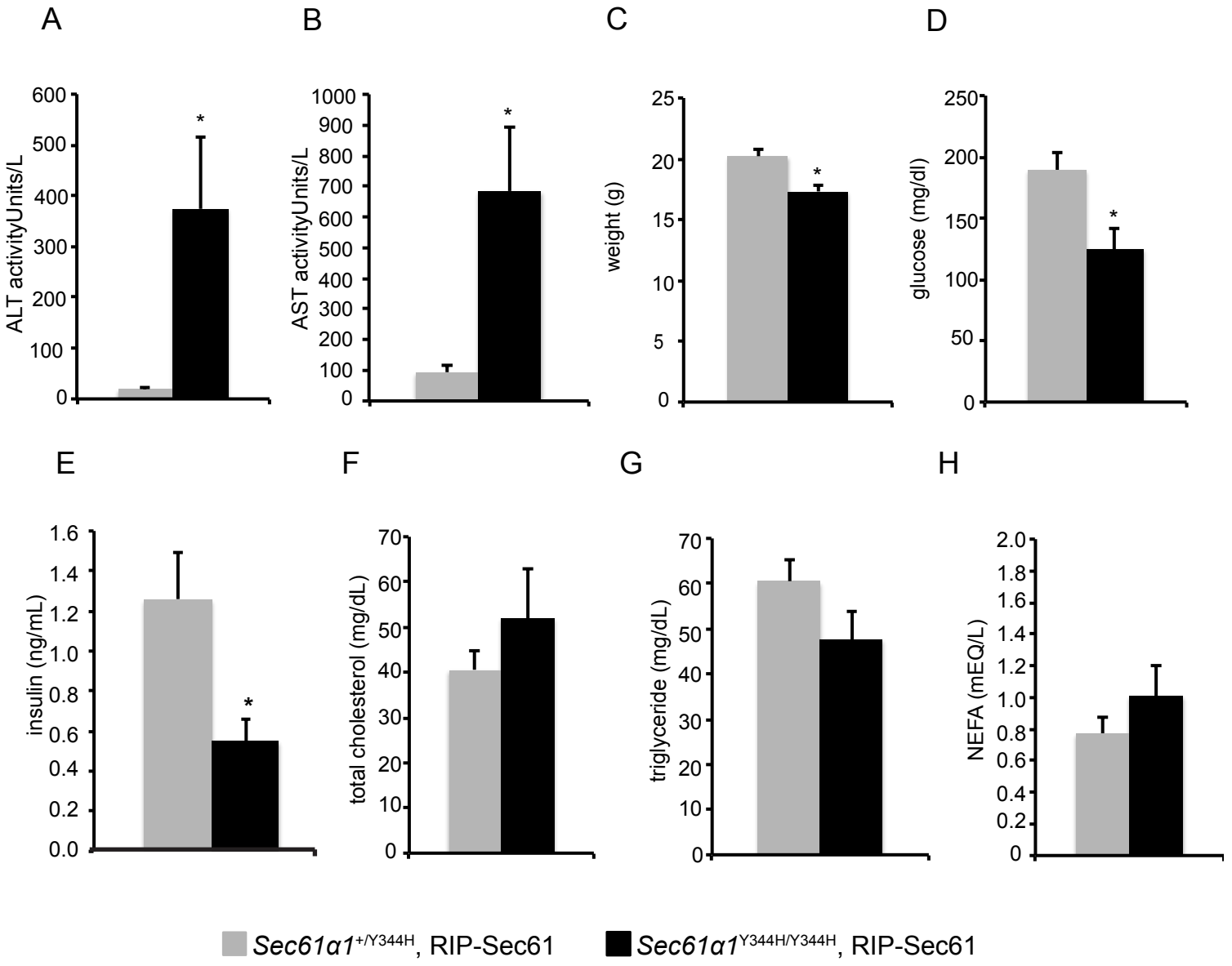

Fig. S1. (A-H) Analysis of weight and plasma metabolites in age- and sex-matched, fasted *Sec61α1*$^{+/Y334H}$, RIP-Sec61 (n=7) and *Sec61α1*$^{Y344H/Y334H}$, RIP-Sec61 (n=6) mice: (A) ALT, (B) AST, (C) Weight, (D) glucose, (E) insulin, (F) total cholesterol, (G) triglycerides and (H) non-esterified fatty acids. Error bars represent SEM and * indicates p≤0.05.

Figure S2

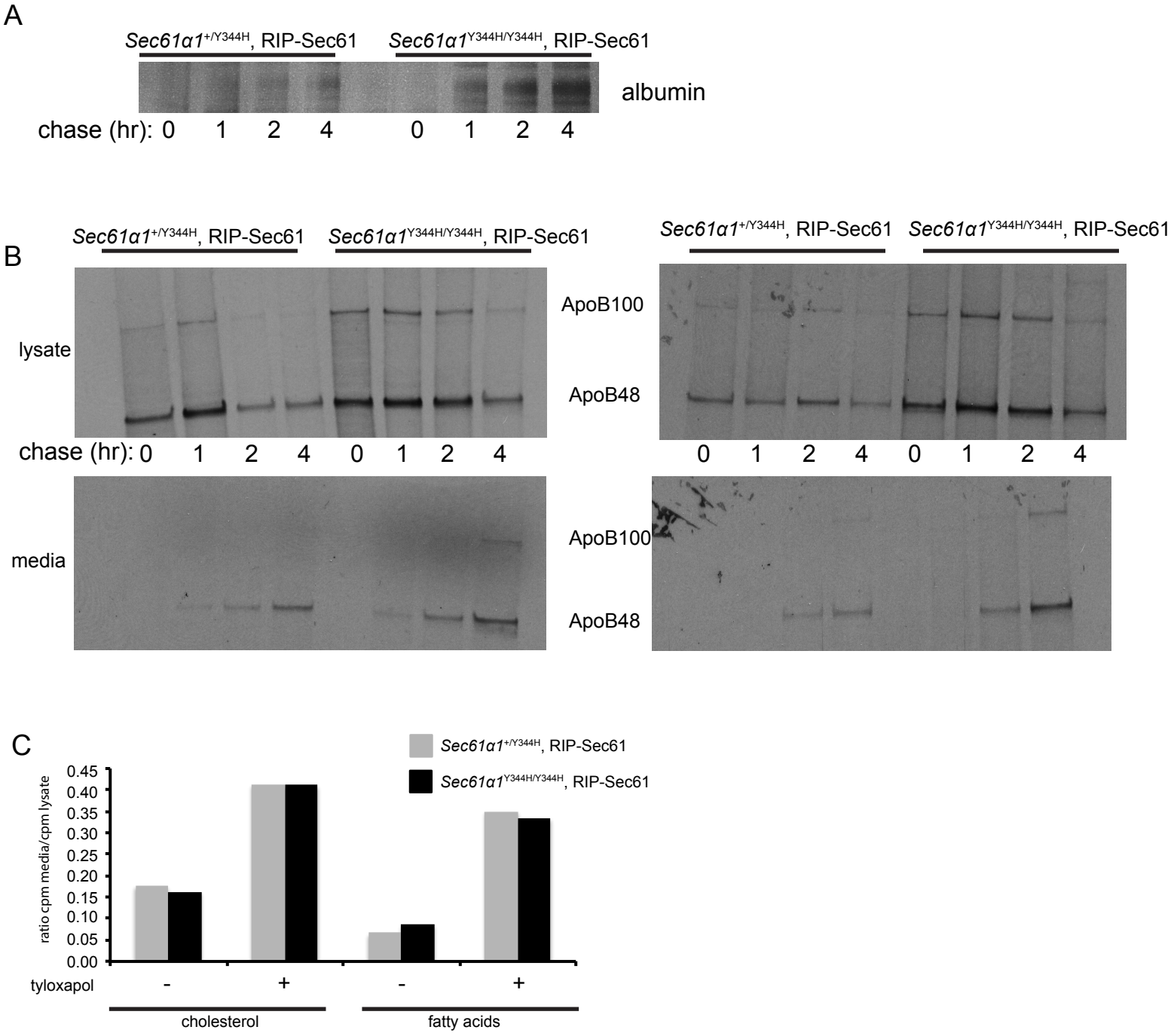

Fig. S2. Normal lipoprotein and lipid secretion in hepatocytes from *Sec61a1*$^{Y344H/Y344H}$, RIP-Sec61 mice. Primary hepatocytes were isolated from age- and sex-matched, fasted mice of the indicated genotypes. (A) Silver stain gel of culture media from cells after washing three times with PBS, and incubating in serum-free media for the indicated times. (B) Analysis of ApoB secretion in primary hepatocytes labeled with ^{35}S cysteine and methionine for one hour and chased for the indicated times. (C) Primary hepatocytes were labeled for 16 hours with ^{14}C-acetate, washed 3 times with PBS, and then incubated for 1 hour in serum-free media with or without 0.01% tyloxapol, which inhibits lipoprotein lipase to prevent lipid re-uptake. Sterol and triglyceride fractions were then extracted from media and cell lysate and analyzed by scintillation counting. The assay was performed in triplicate. Counts in cell culture media were normalized to cell-associated counts.

Figure S3

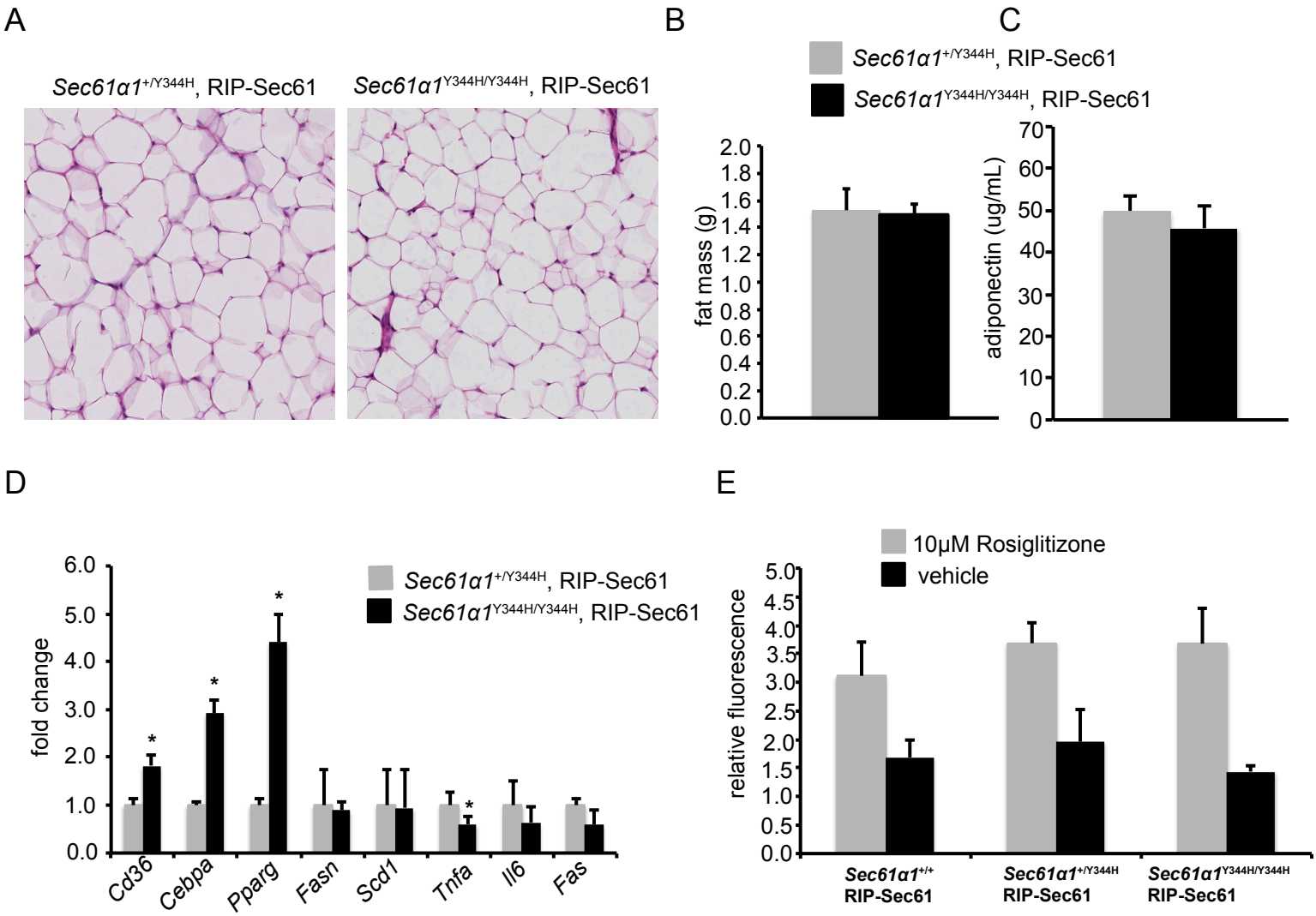

Fig. S3. *Sec61a1$^{Y344H/Y344H}$*, RIP-Sec61 mice have normal adipose tissue.
(A) H&E stained adipose tissue sections at 20x magnification. (B) Fat mass measurement obtained via Echo MRI (Sec61α1$^{+/Y334H}$, RIP-Sec61, n=7; Sec61α1$^{Y344H/Y334H}$, RIP-Sec61, n=6). (C) Plasma adiponectin levels (Sec61α1$^{+/Y334H}$, RIP-Sec61, n=7; Sec61α1$^{Y344H/Y334H}$, RIP-Sec61, n=6). (D) qPCR analysis of RNA from adipose tissue (n=4 per genotype). (E) Differentiation of MEFs into adipocytes as measured by accumulation of Adipored fluorescence (Sec61α1$^{+/+}$, RIP-Sec61, n=4; Sec61α1$^{+/Y334H}$, RIP-Sec61, n=2; Sec61α1$^{Y344H/Y334H}$, RIP-Sec61, n=2). Error bars represent SEM and * indicates p≤0.05.

Figure S4

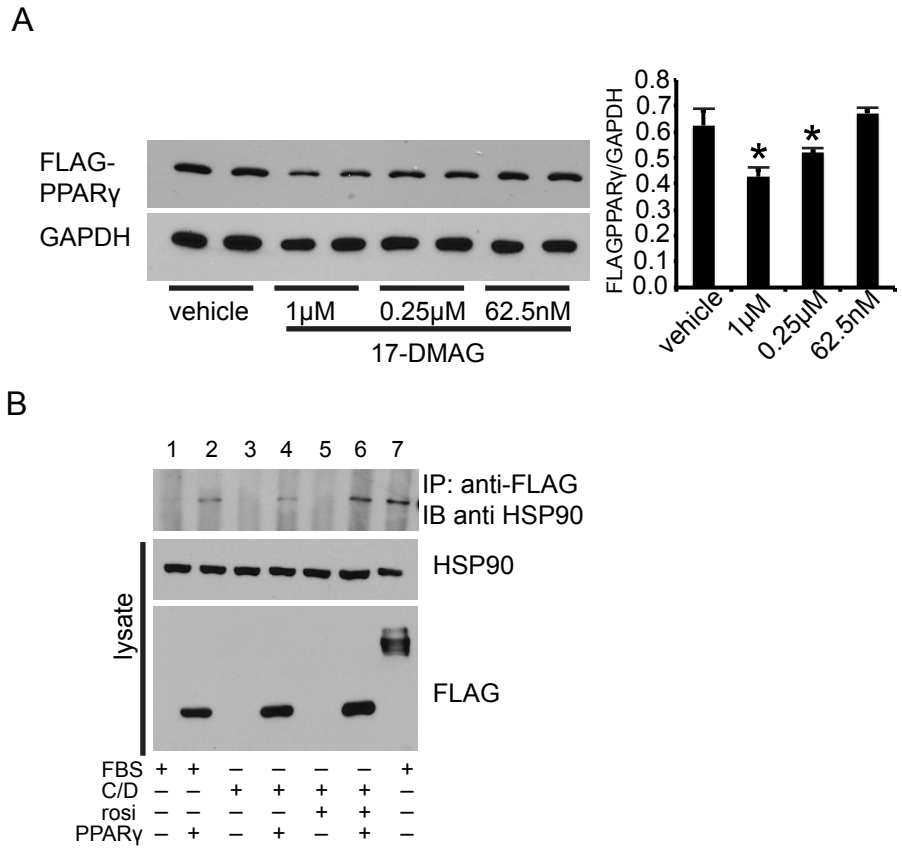

Fig. S4. Inhibition of Hsp90 reduces Pparγ protein levels.
A: Western blot analysis of HEK293 cells transfected with a CMV-FLAG-Pparγ treated with the indicated concentrations of 17-DMAG for 16 hours. Densitometry is shown to the right. B: Western blot analysis of immunoprecipitates and lysates from HEK293 cells treated as indicated and transfected with vector (lanes 1,3 and 5), CMV:FLAG-Pparγ (lane 2,4 and 6) or FLAG-tagged Hsf1 (lane 7, positive control for a known Hsp90 interactor).