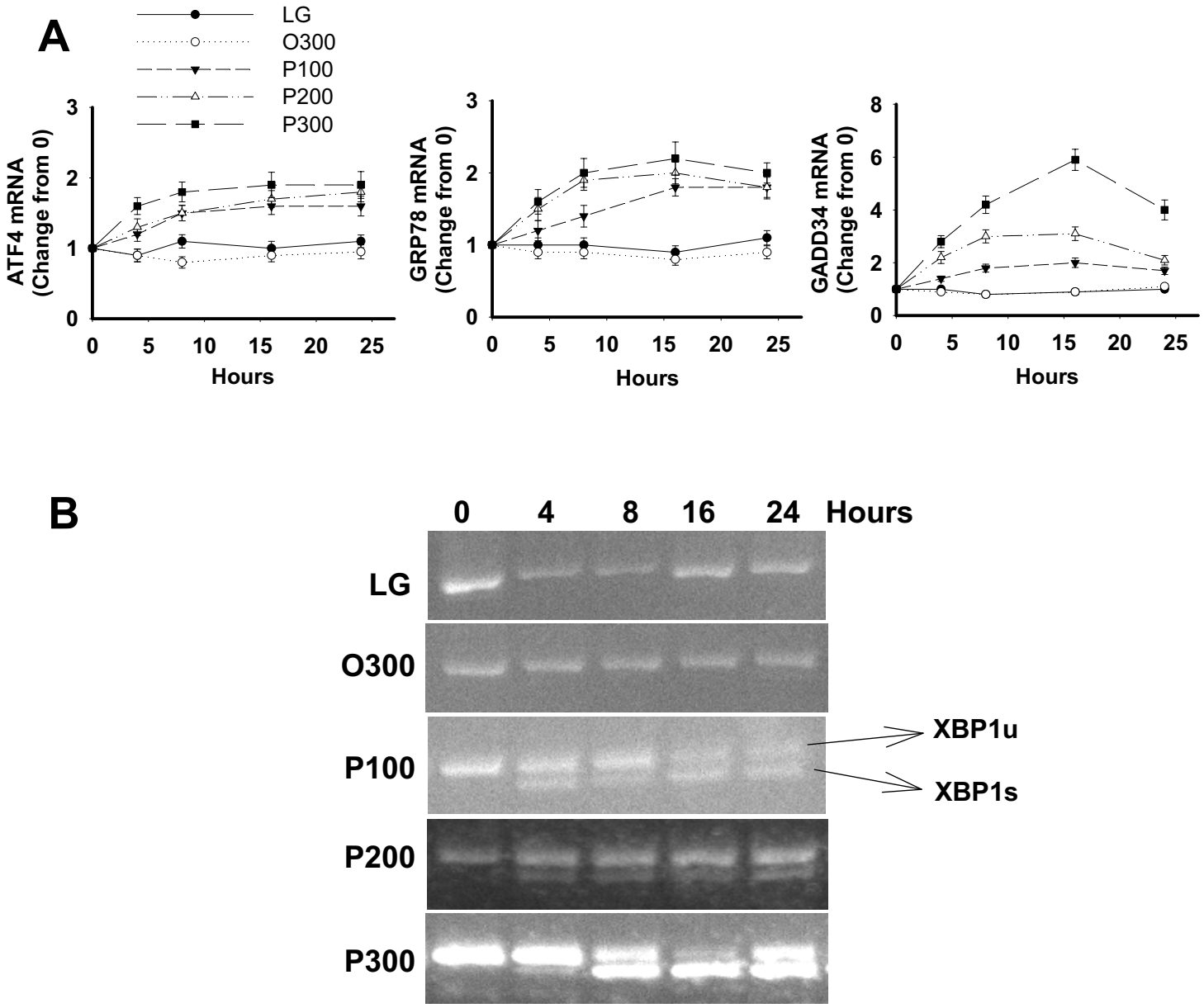
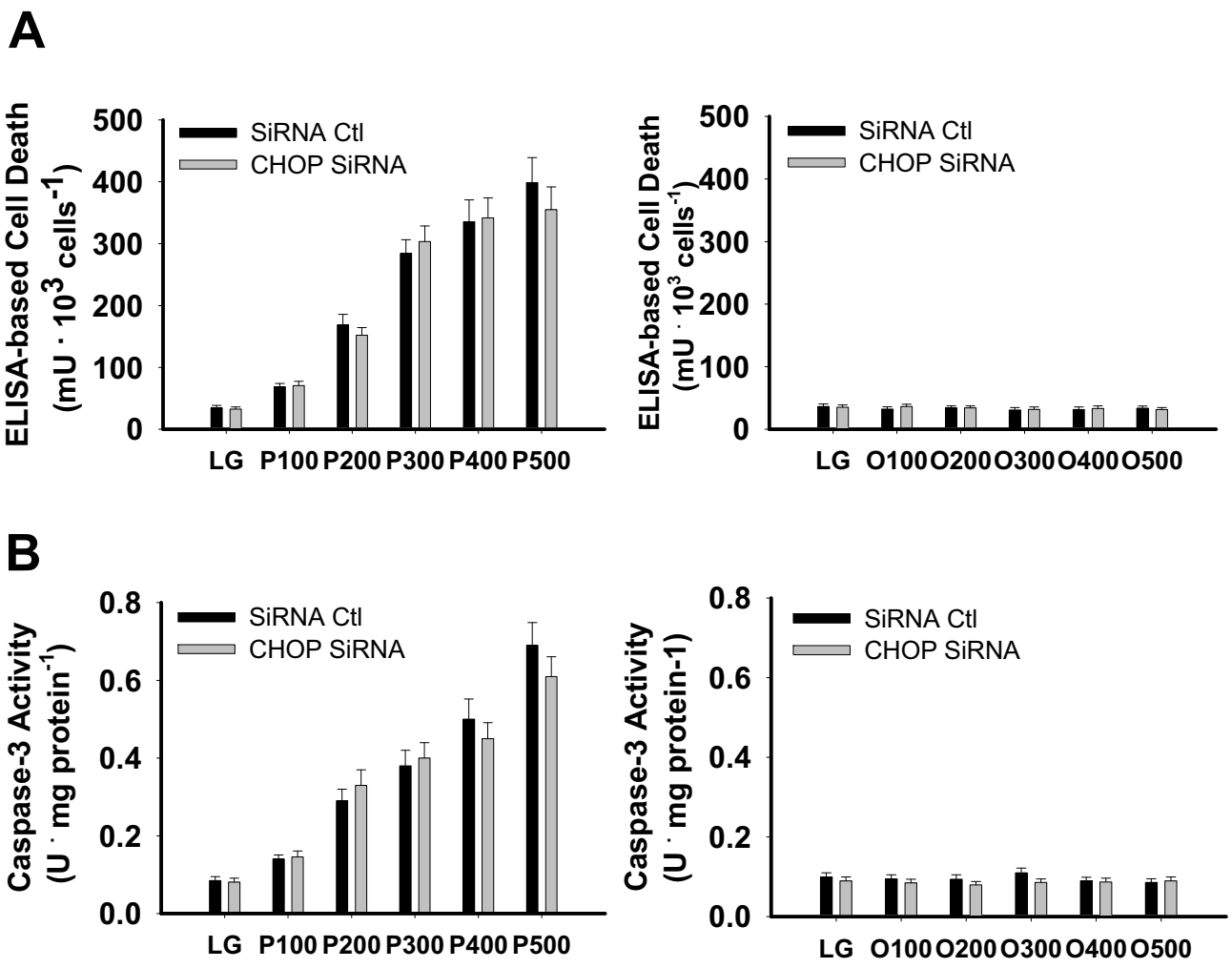


Supplemental Figure 1



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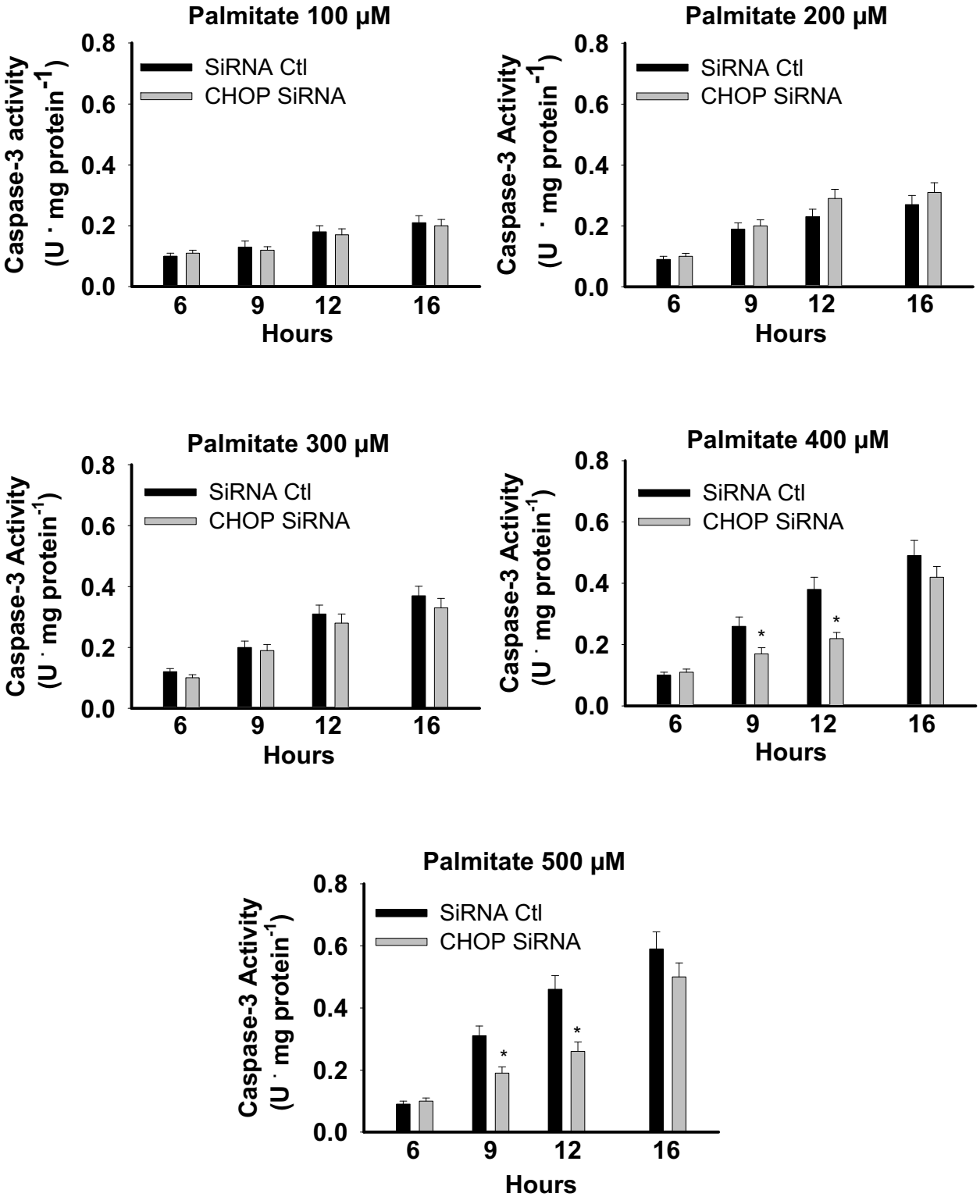
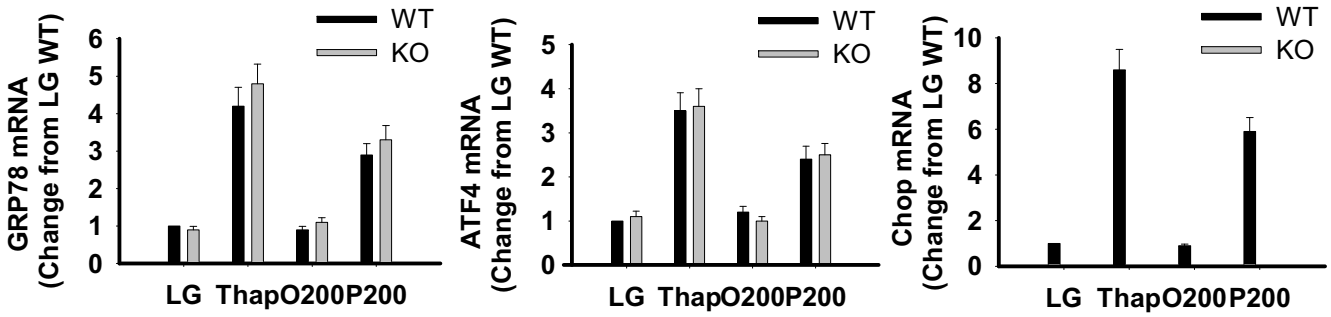
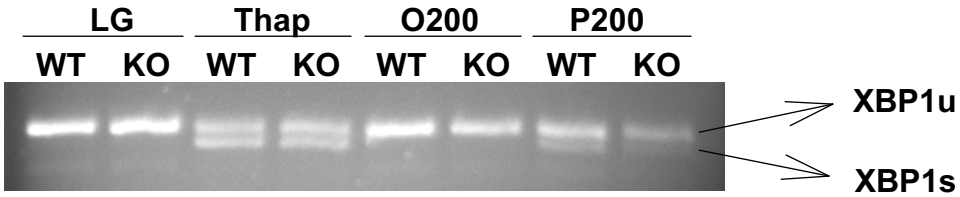
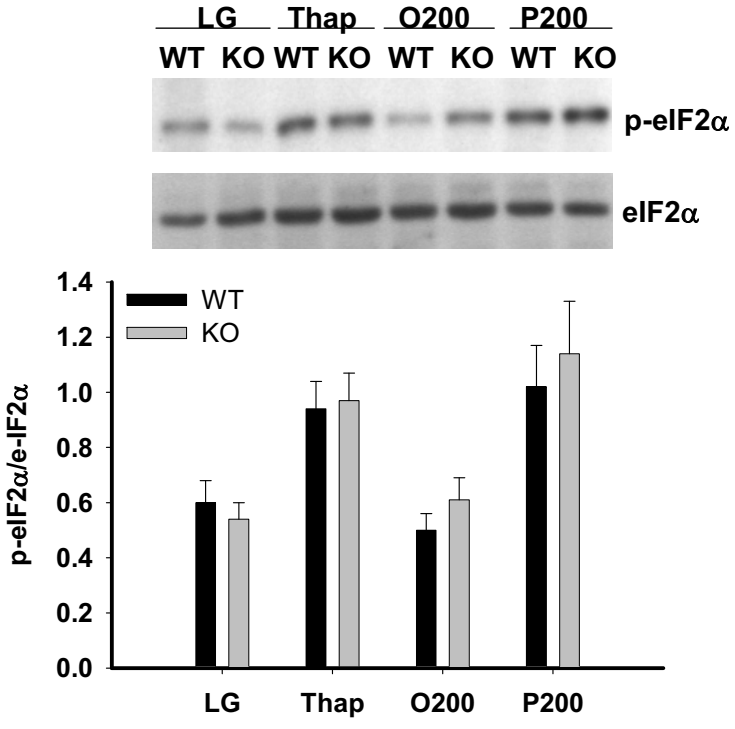


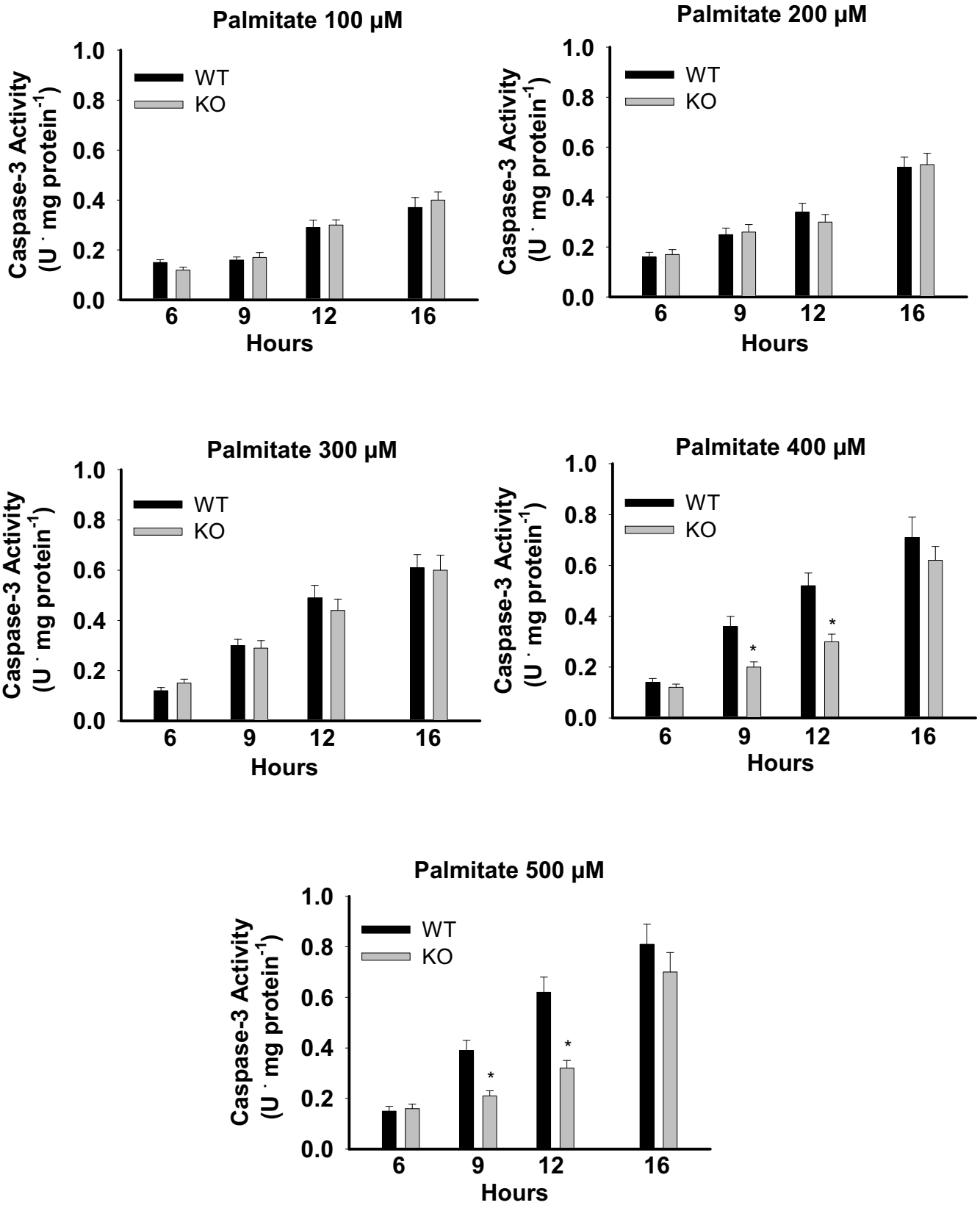
Supplemental Figure 3



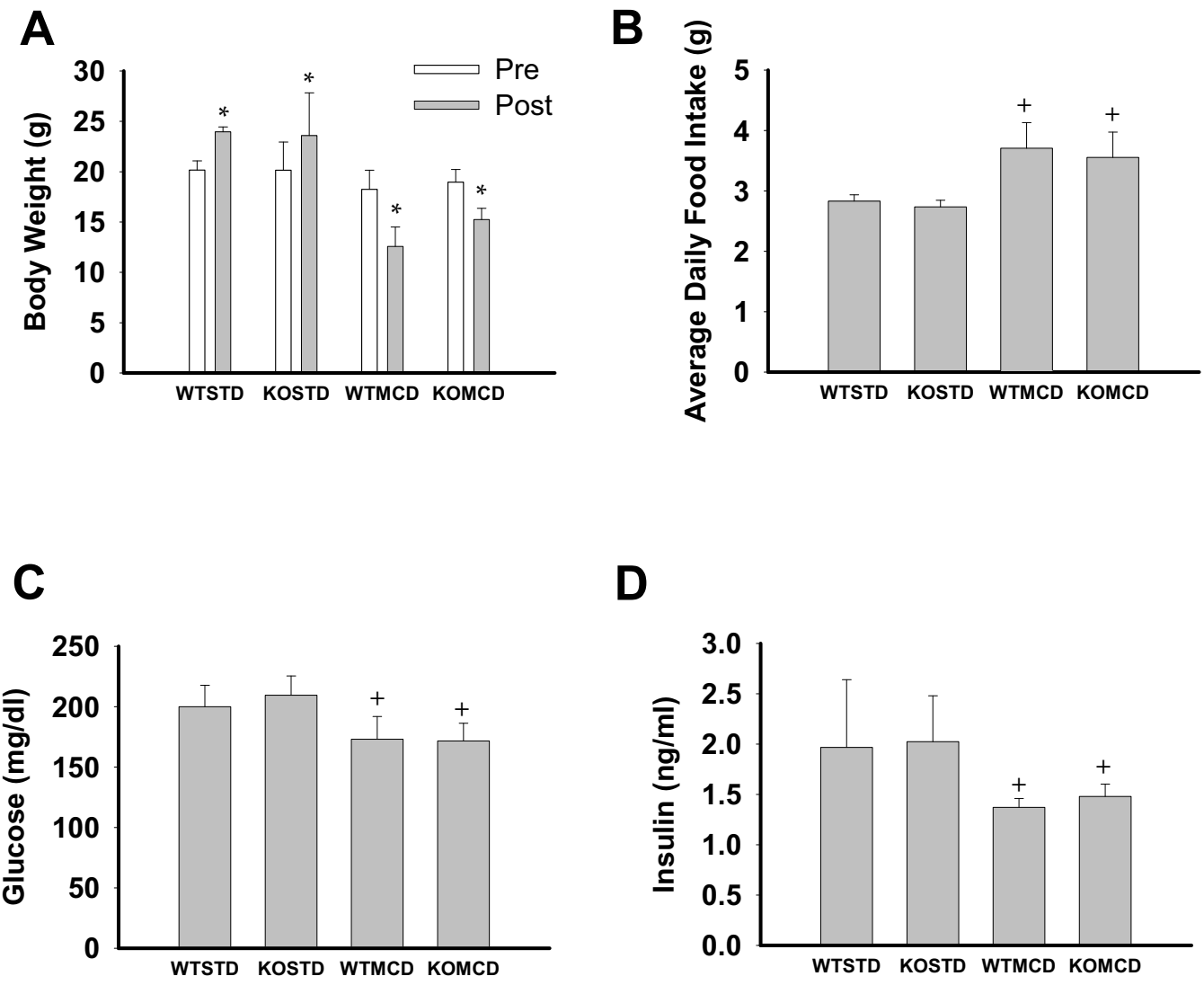




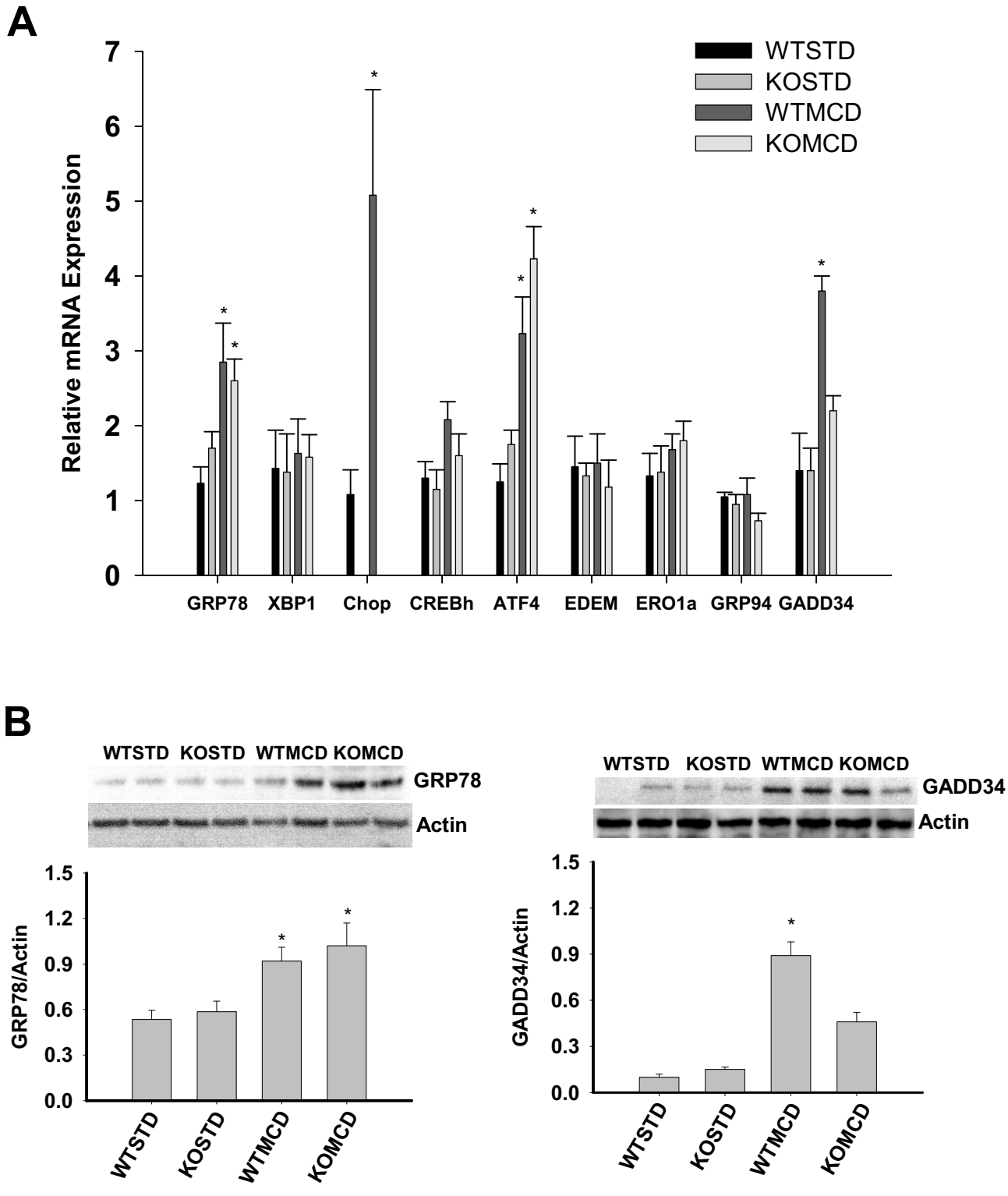
Supplemental Figure 4



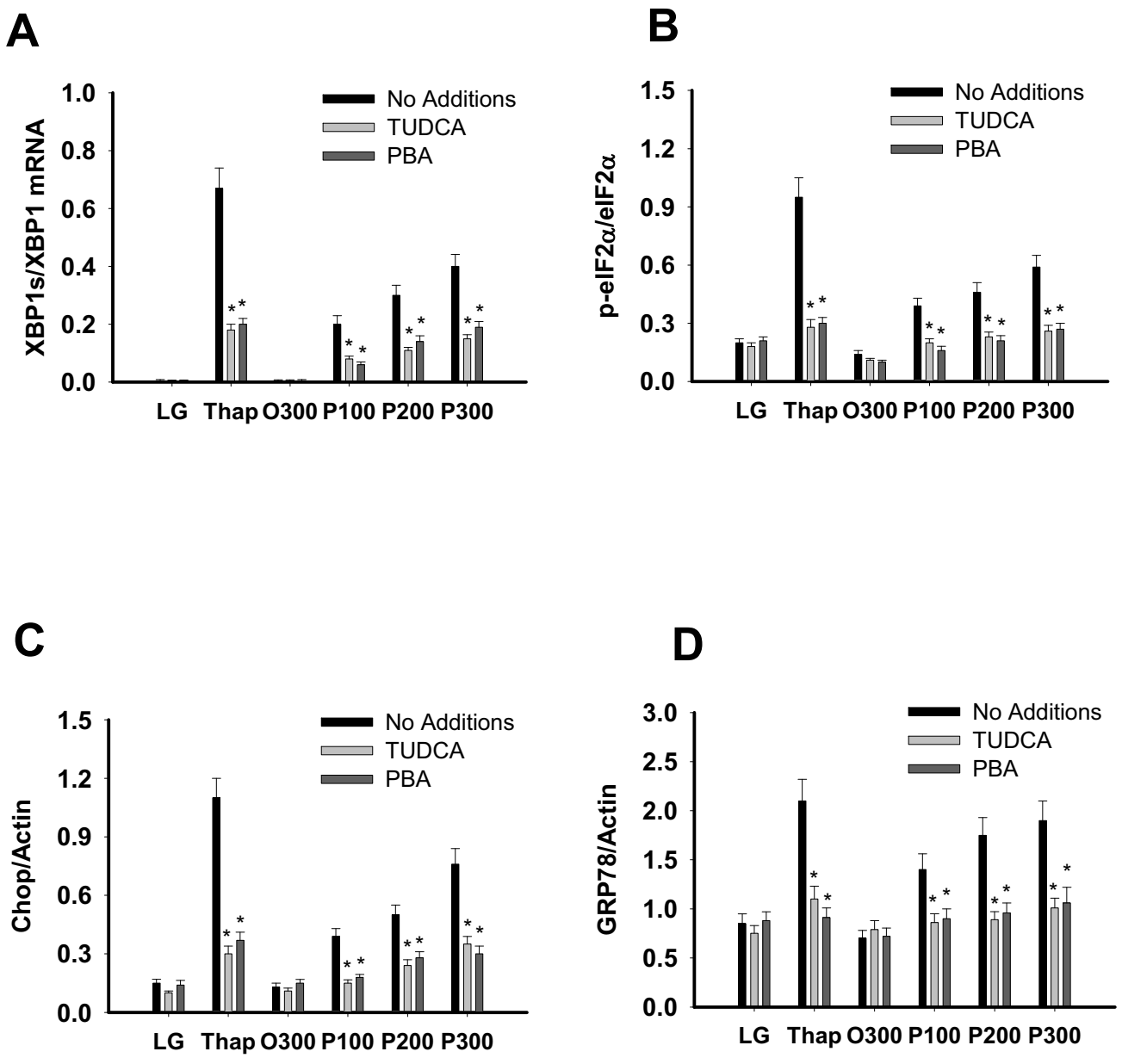
Supplemental Figure 5



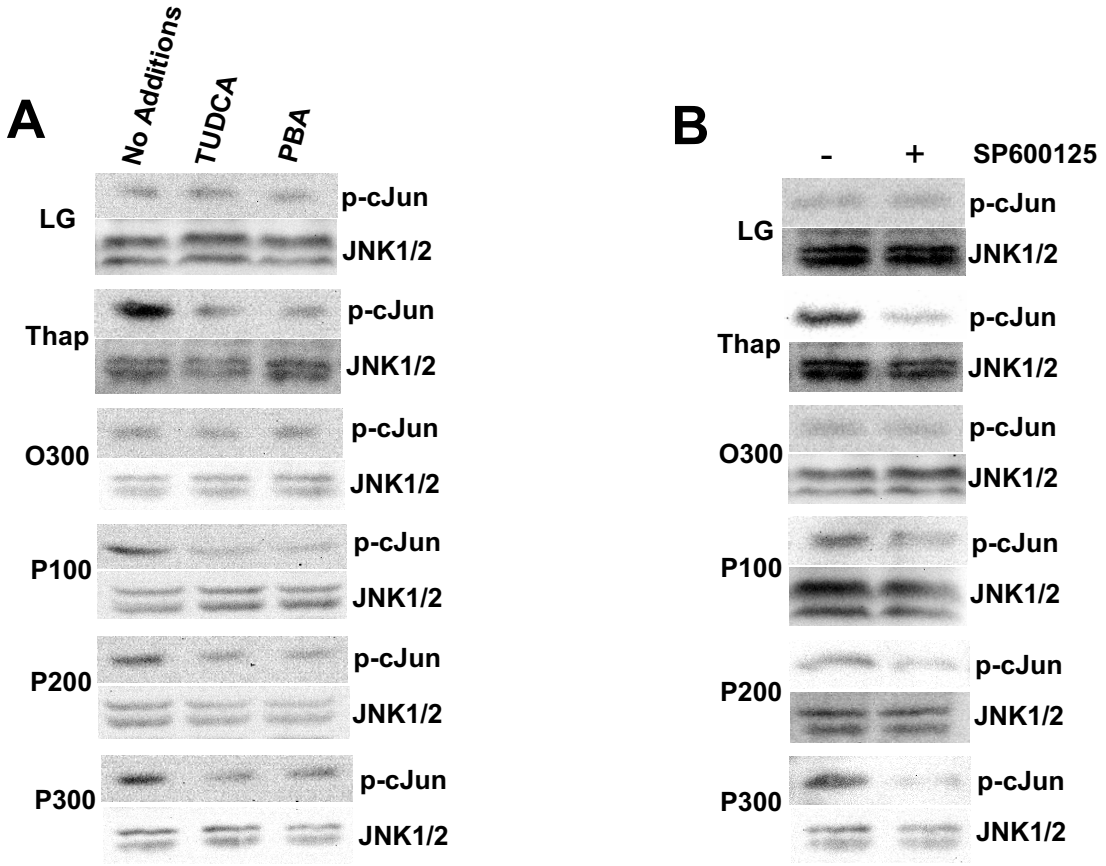
Supplemental Figure 6



Supplemental Figure 7



Supplemental Figure 8



Supplemental Figure 9

Supplemental Figure Legends

Supplemental Figure 1. ER stress markers and caspase-3 activity in H4IIE liver cells. H4IIE liver cells were incubated for varying periods of time in control media (LG), or control media supplemented with albumin-bound oleate at 300 μM (O300) or palmitate at 100 (P100), 200 (P200), or 300 μM (P300). Activating transcription factor-4 (ATF4), glucose regulated protein 78 (GRP78), growth arrest and DNA damage inducible gene 34 (GADD34), unspliced (u) and spliced (s) X-box binding protein-1 (XBP1), and caspase-3 activity. Data in graphs are reported as the mean ± SD for n=5-7 group. XBP1 gel is representative of 5-7 independent experiments.

Supplemental Figure 2. Dose-response studies in H4IIE liver cells. H4IIE liver cells were transfected with control SiRNA or *Chop* SiRNA as described in materials and methods and then incubated for 16 hrs in control media (LG), or control media supplemented with albumin-bound palmitate (P) or oleate (O) at concentrations of 100, 200, 300, 400, 500 μM. Cell integrity was assessed by ELISA and caspase-3 activity. Data in graphs are reported as the mean ± SD of triplicate samples from 6 independent experiments.

Supplemental Figure 3. Time course studies in H4IIE liver cells to assess caspase-3 activity. H4IIE liver cells were transfected with control SiRNA or *Chop* SiRNA as described in materials and methods and then incubated in the presence of varying palmitate concentrations for durations of 6, 9, 12, and 16 hrs. Data in graphs are reported as the mean ± SD of triplicate samples from 6 independent experiments.

Supplemental Figure 4. ER stress markers in primary hepatocytes from wild type (WT) and *Chop* knockout (KO) mice. Primary hepatocytes were incubated in control media (LG) or control media supplemented with thapsigargin (450 nM), albumin-bound oleate at 200 μM (O200) or albumin-bound palmitate at 200 μM (P200) for 16 hrs. Glucose regulated protein 78 (GRP78), activating transcription factor-4 (ATF4), Chop, and unspliced (u) and spliced (s) X-box binding protein 1 (XBP1) mRNA; and phosphorylated (p) and total eukaryotic initiation factor 2α (eIf2α) from liver samples. Data in graphs are reported as the mean ± SD of triplicate samples from 6 independent experiments. XBP1 and eIF2α gels are representative of 6 independent experiments.

Supplemental Figure 5. Time course and dose-response studies in primary hepatocytes from wild type (WT) and *Chop* knockout (KO) mice to assess caspase-3 activity. Primary hepatocytes were incubated in the presence of varying palmitate concentrations for durations of 6, 9, 12, and 16 hrs. Data in graphs are reported as the mean ± SD of triplicate samples from 6 independent experiments.

Supplemental Figure 6. Body weight and plasma measures in wild type and *Chop* knockout (KO) mice. Wild type and Chop knockout mice were provided a purified high starch diet (STD) or a methionine-choline deficient (MCD) diet for 3 weeks. (A) Body weight, (B) food intake, (C) plasma glucose and (D) plasma insulin. Plasma glucose and insulin levels reflect values in 6-8 hrs fasted mice. Values are reported as the mean ± SD for n=6 per group. *, significantly ($P < 0.05$) different from Pre. +, significantly ($P < 0.05$) different from STD.

Supplemental Figure 7. ER stress markers in liver from wild type and *Chop* knockout (KO) mice. Wild type and *Chop* knockout mice were provided a purified high starch diet (STD) or a methionine-choline deficient (MCD) diet for 3 weeks. (A) Glucose regulated protein 78 (GRP78), X-box binding protein 1 (XBP1), CCAAT-homologous protein (Chop), CRE-binding protein hepatic (CREBh), activating transcription factor-4 (ATF4), endoplasmic reticulum mannosidase (EDEM), endoplasmic reticulum oxidase-1α (ERO1a), glucose regulated protein 94 (GRP94), and growth arrest and DNA damage-inducible gene 34 (GADD34) mRNA and (B) GRP78 and GADD34 protein from liver samples. Data in graphs are reported as the mean ± SD for n=6 per group. *, significantly ($P < 0.05$) different from STD.

Supplemental Figure 8. ER stress markers in primary hepatocytes isolated from wild type mice. Primary hepatocytes were incubated in control media (LG) or control media supplemented with thapsigargin (450 nM), albumin-bound oleate at 300 μM (O300) or albumin-bound palmitate at 100 μM (P100), 200 μM (P200) or 300 μM (P300) in the absence or presence of chemical chaperones, taurine-conjugated ursodeoxycholic acid (TUDCA, 200 μM) or 4-phenylbutyric acid (PBA, 500 μM) for 16 hrs. (A) ratio of spliced (s) to unspliced X-box binding protein 1 (XBP1) mRNA, (B) ratio of phosphorylated (p) eukaryotic initiation factor-2α (eIF2α) to total eIF2α by western blot, (C) ratio of C/EBP homologous protein (Chop) to actin by western blot, (D) ratio of glucose regulated protein 78 (GRP78) to actin by western blot. Data in graphs are reported as the mean ± SD for n=6 per group. *, significantly ($P < 0.05$) different from No Addition.

Supplemental Figure 9. Representative western blots for phosphorylation of c-Jun (p-cJun) and total JNK (JNK1/2) and cell survival (MTT assay) in primary hepatocytes. Primary hepatocytes

were incubated in control media (LG) or control media supplemented with thapsigargin (450 nM), albumin-bound oleate at 300 μM (O300) or albumin-bound palmitate at 100 μM (P100), 200 μM (P200) or 300 μM (P300) in the absence or presence of chemical chaperones, taurine-conjugated ursodeoxycholic acid (TUDCA, 200 μM) or 4-phenylbutyric acid (PBA, 500 μM) or SP600125 for 16 hrs. Data in graphs are reported as the mean ± SD for n=6 per group. *, significantly ($P < 0.05$) different from –SP600125.