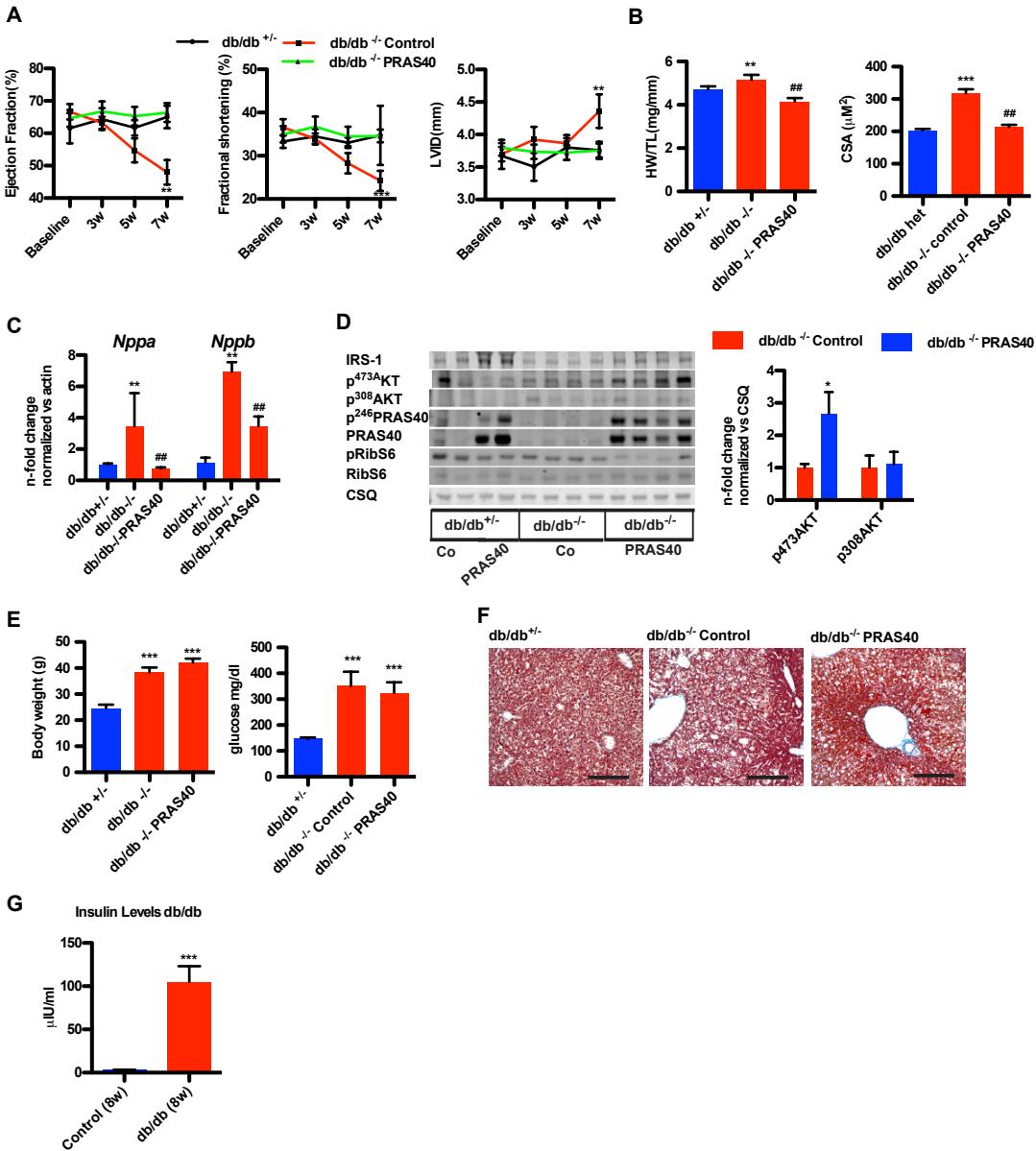


or AAV-PRAS40 injected animals. (C) Confocal microscopy of paraffin-embedded liver sections after AAV-PRAS40 injections stained for FLAG-tag (red), Actin (green) and nuclei (blue). Only single cells are positive for the FLAG-tag.

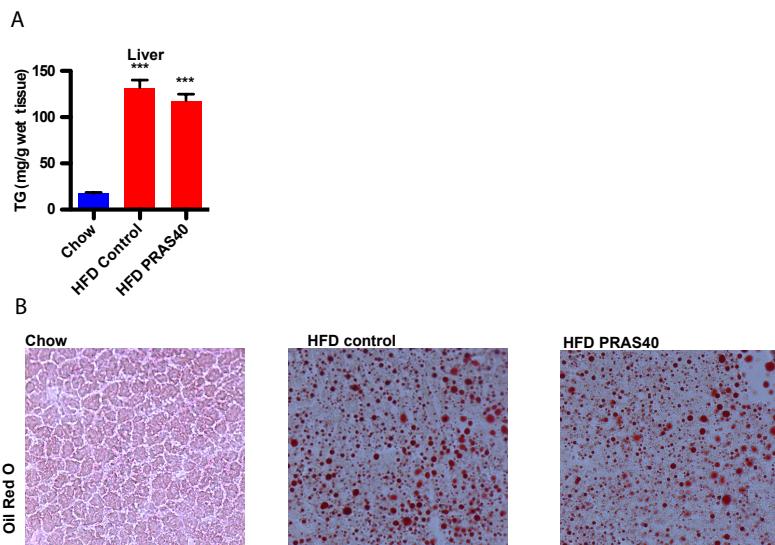
**Supporting Figure 3**



**Supporting Figure 3. PRAS40 prevents diabetic cardiomyopathy in db/db mice. (A)** Line graphs representing echocardiographic assessment of heterozygous control or *db/db* mice for percentage of fractional shortening (FS), ejection fraction (EF) and end-diastolic dimension (LVID), \*\*p<0.01 vs control *db/db*. n=4 per het and 6 per *db/db* group. **(B)** Heart weight to tibia length ratio (HW/TL) in the indicated groups.. (\*\*p<0.01 versus control het; ##p<0.01 versus

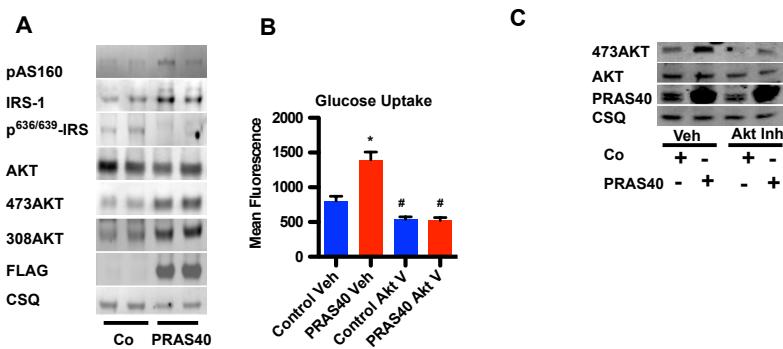
control *db/db*). CSA in control and PRAS40 mice (\*\*p<0.01 versus control het; ##p<0.01 versus control *db/db*). (C) *Nppa* and *Nppb* levels (\*\*p<0.01 versus control het; ##p<0.01 versus control *db/db*). (D) Immunoblots of whole heart lysates. Barplots depicting quantitation of Akt phosphorylation. \*p<0.05 versus control. (E) Body weight and glucose levels in the indicated groups \*\*\*p<0.01 vs hets. (F) Mason-Trichrome staining of liver sections in the indicated groups. Scale bar 150 $\mu$ m (G) Blood insulin levels in the indicated groups. \*\*\*p<0.01 vs controls. n=5 in each group.

**Supporting Figure 4**



**Supporting Figure 4.** (A) TG content in the liver \*\*\*p<0.01 versus control chow. (B) Lipid accumulation evidenced by Oil Red O staining. Scale bar 150 $\mu$ m.

**Supporting Figure 5**



**Supporting Figure 5.** (A) IRS-1 degradation is prevented and Akt phosphorylation is