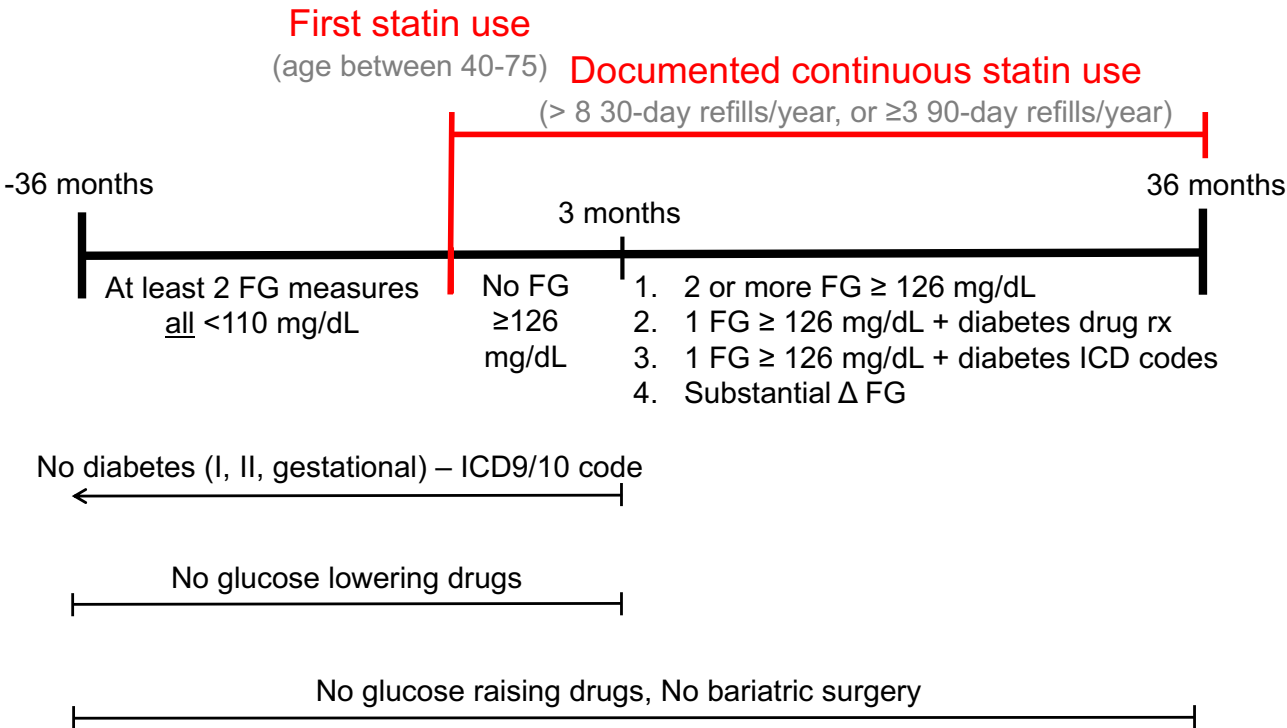
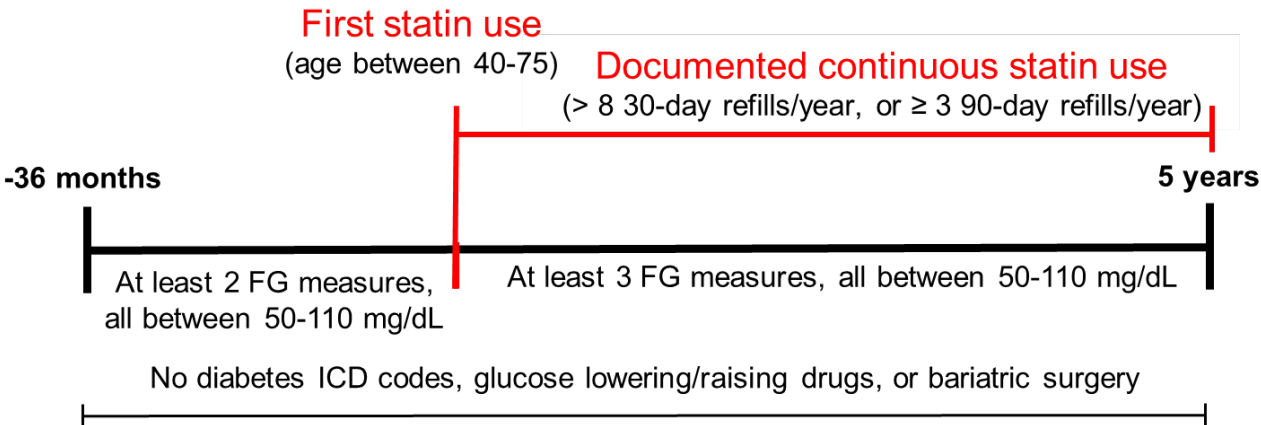


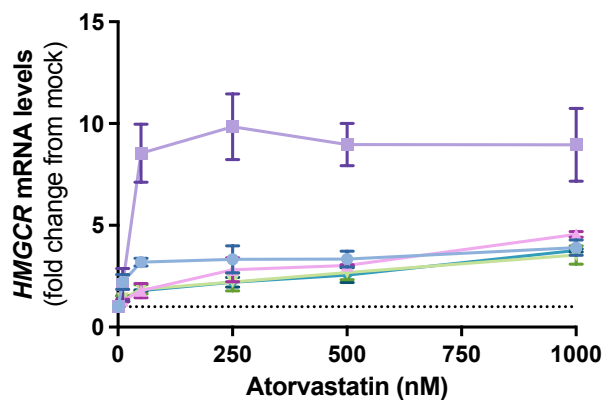
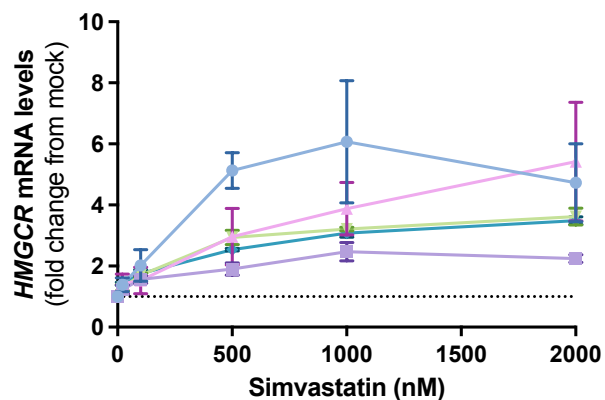
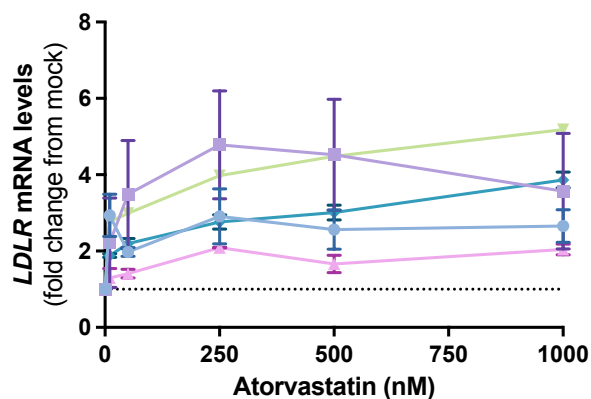
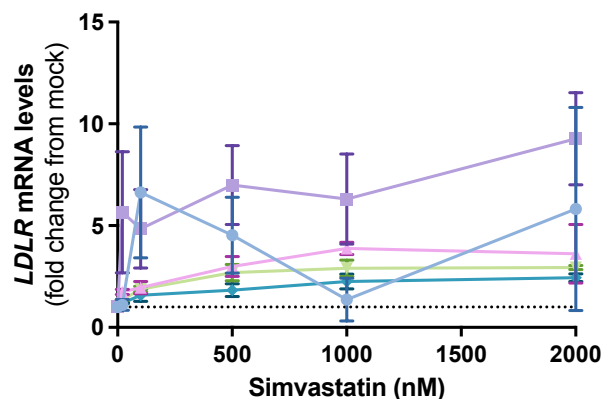
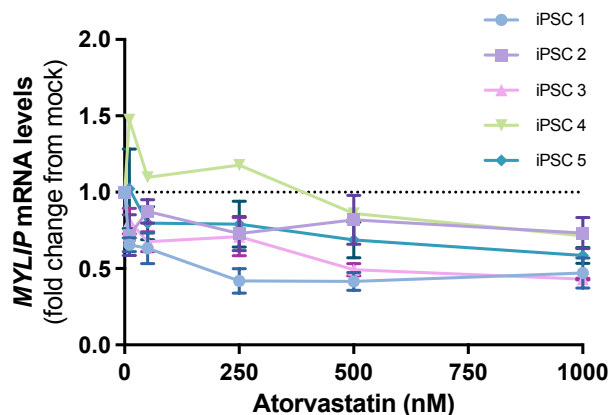
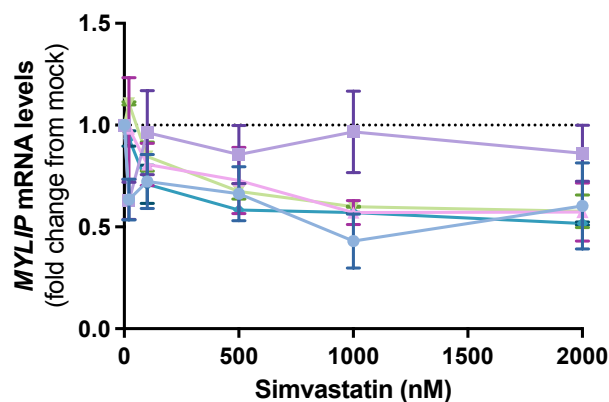
# A NOD Susceptible Cases



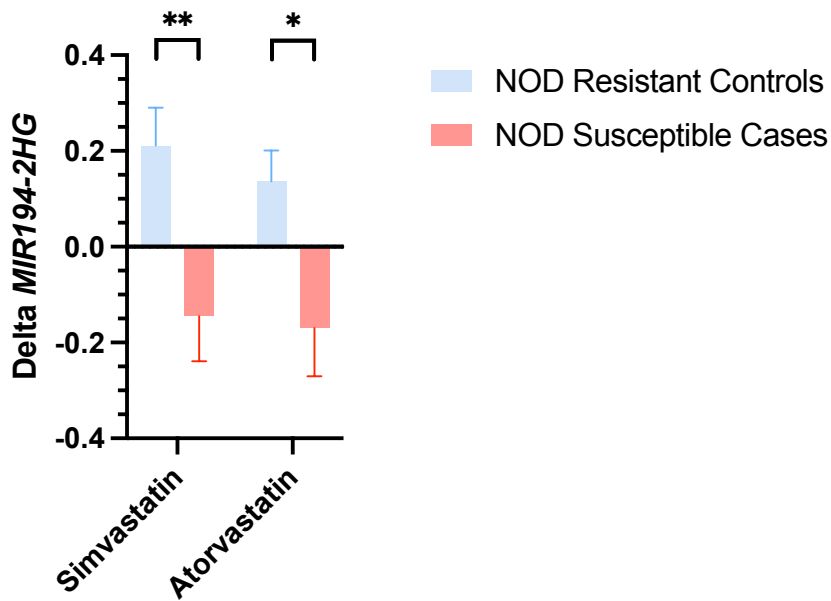
# B NOD Resistant Controls



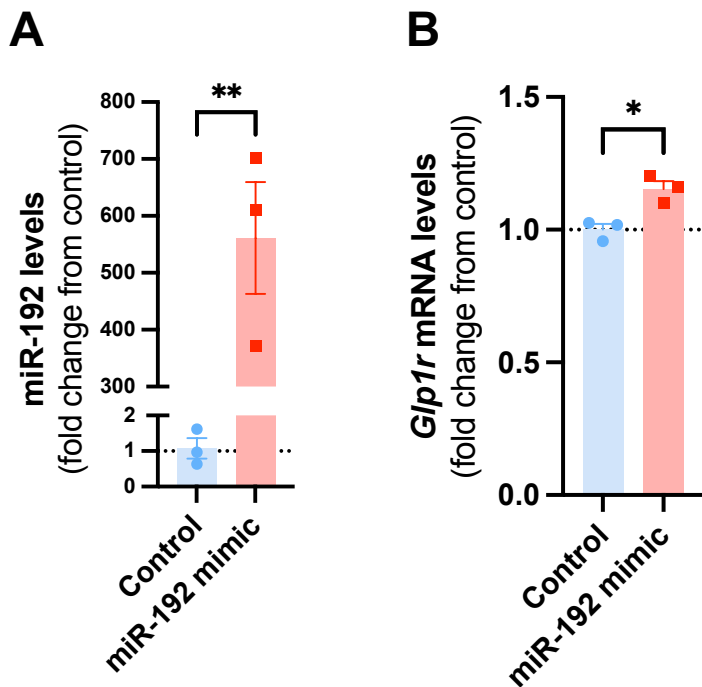
**Supplementary Figure 1. Algorithm used to identify statin-induced new-onset diabetes (NOD) susceptible case (A) or NOD resistant control (B) cohorts from the electronic databases of the Kaiser Permanente of Northern California.** Abbreviations: FG, fasting glucose; ICD, international classification of diseases; rx, prescription.

**A****B****C**

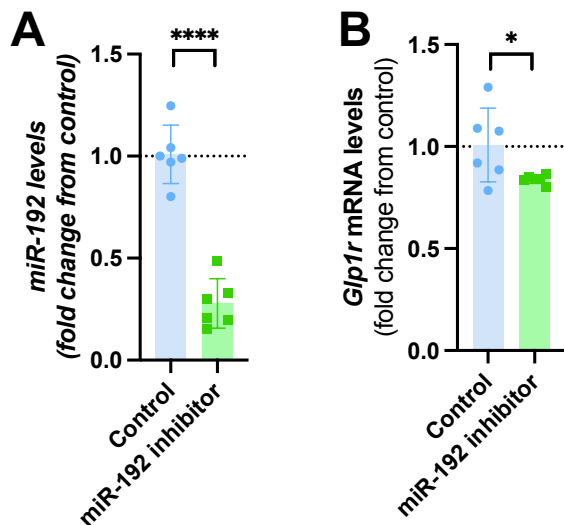
**Supplementary Figure 2. Statin dose response on *HMGCR* and *MYLIP* expression in iPSC.** Five iPSC lines were treated with a wide concentration range of simvastatin and atorvastatin for 24 hours before *HMGCR* (A), *LDLR* (B), and *MYLIP* (C) transcript levels were quantified by qPCR and normalized to *CLPTM1*. Data are presented as mean  $\pm$  SEM.



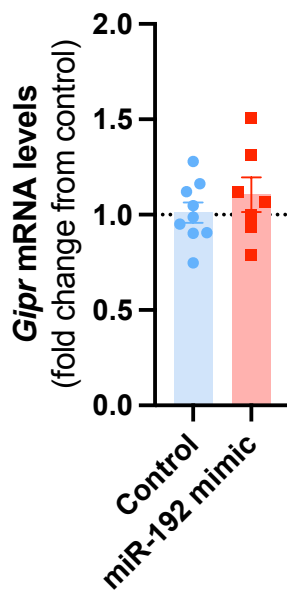
**Supplementary Figure 3.** Change in *MIR194-2HG* levels in iPSCs derived from statin users whose pre-statin fasting glucose levels were less than 100 mg/dL and categorized as NOD susceptible cases (n=19 for atorvastatin treatment and n=18 for simvastatin treatment due to one sample failing library construction ) or NOD resistant controls (n=13) after 24 hour incubation with 500 nM simvastatin, 250 nM atorvastatin or mock control buffer. Values were variance stabilized ( $\sim\log_2$  transformation) in DESeq2 and deltas were calculated as statin-control expression levels. Data are presented as mean  $\pm$  SEM. Statistical significance was determined by unpaired t-test, \* $p < 0.05$ , \*\* $p < 0.01$ .



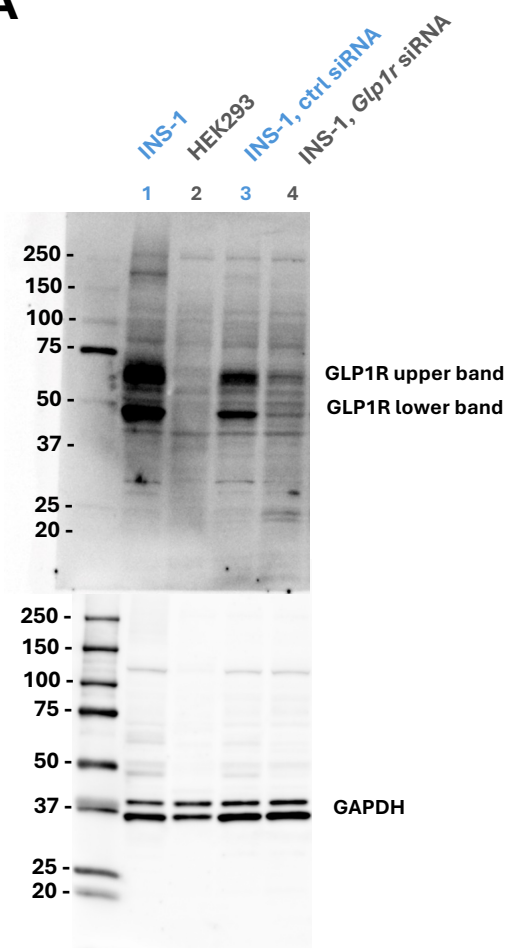
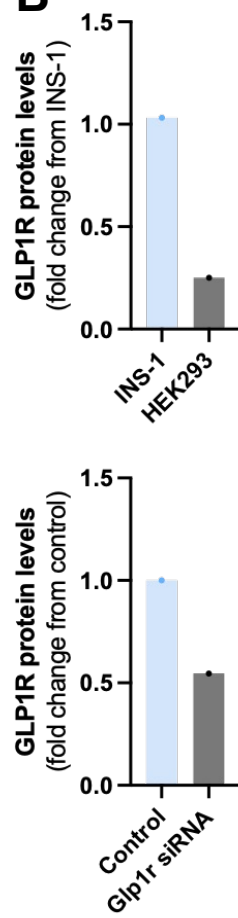
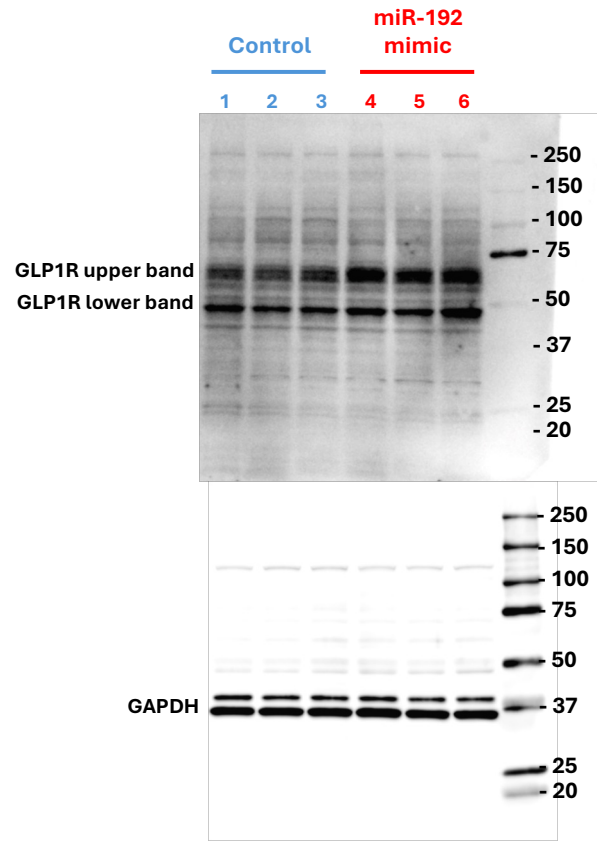
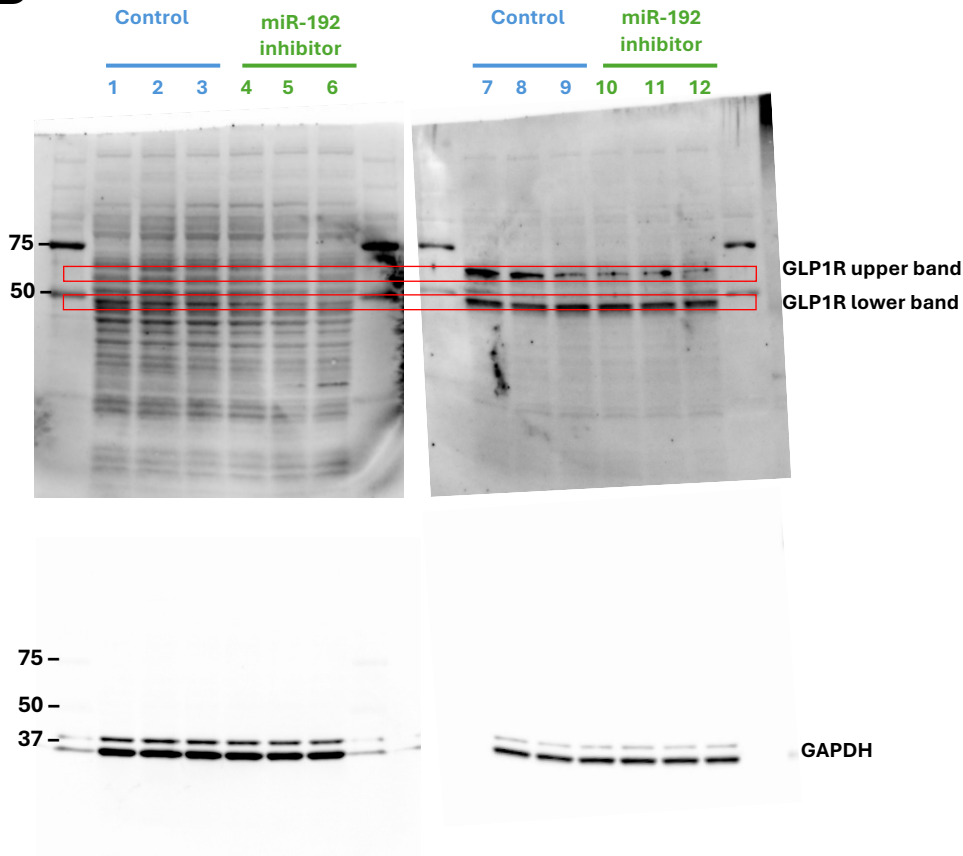
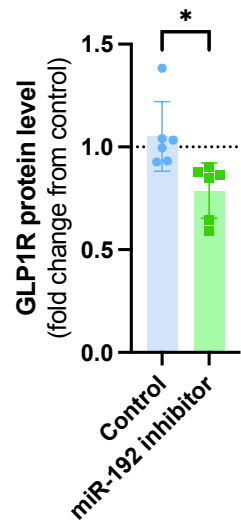
**Supplementary Figure 4. miR-192 upregulates *Glp1r* transcript levels in  $\beta$ TC3 cells.**  $\beta$ TC3 cells were transfected with 10 nM miR-192 mimic or a non-targeting control. After 48 hours, miR-192 (**A**) and *Glp1r* (**B**) transcript levels were quantified by qPCR and normalized to miR-16 and *Clptm1*, respectively. Data are presented as mean  $\pm$  SEM. Statistical significance was determined by unpaired t-test, \* $p < 0.05$ .



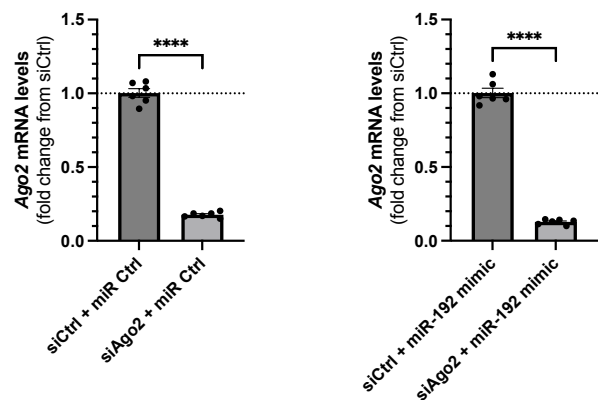
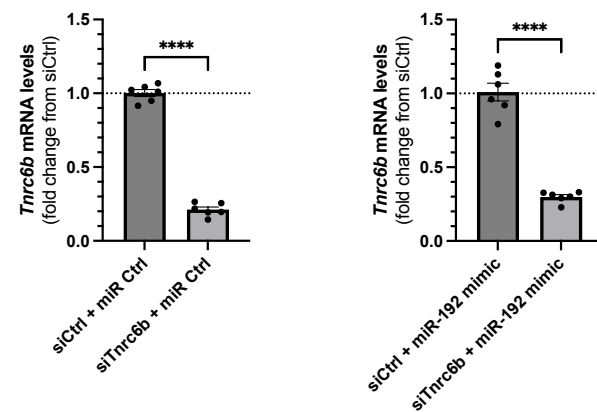
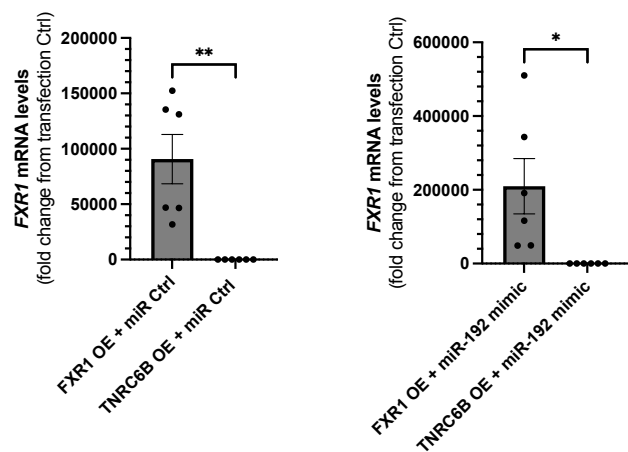
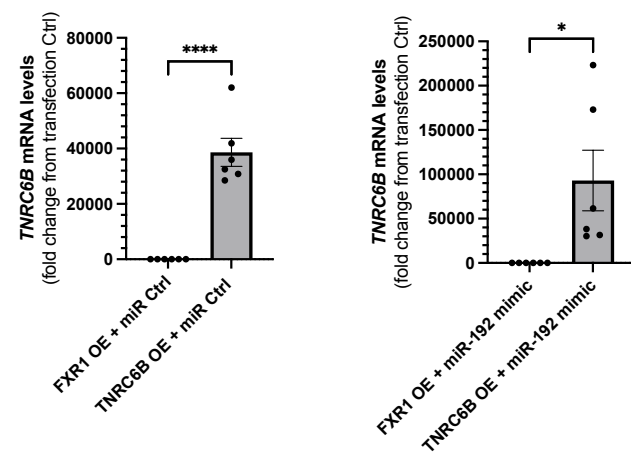
**Supplementary Figure 5. miR-192 inhibitor down-regulates *Glp1r* transcript levels in INS-1 cells.** INS-1 cells were transfected with 30 nM miR-192 inhibitor or a non-targeting control for 48 hours. Transcript levels of miR-192 (**A**) and *Glp1r* (**B**) were quantified by qPCR, and normalized to miR-16 and *Clptm1*, respectively. Data are presented as mean  $\pm$  SEM. Statistical significance was determined by unpaired t-test, \* $p < 0.05$ , \*\*\*\* $p < 0.0001$ .



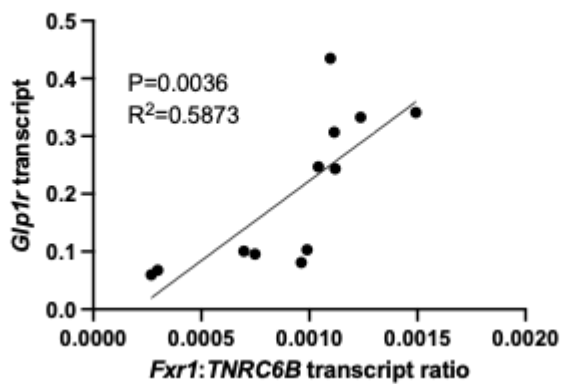
**Supplementary Figure 6. miR-192 regulation of *Gipr* in INS-1.** INS-1 cells were transfected with 10 nM miR-192 mimic or a non-targeting control for 48 hours. *Gipr* transcript levels were quantified by qPCR, normalized to the house keeping gene *Clptm1*. Data are presented as mean  $\pm$  SEM.

**A****B****C****D****E**

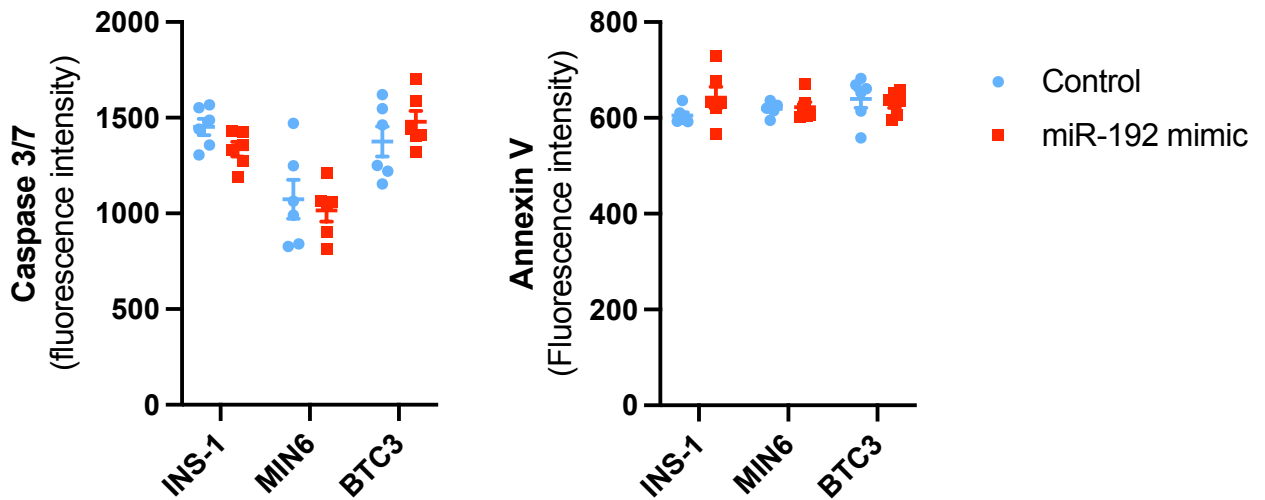
**Supplementary Figure 7. GLP1R antibody validation and western blot images. (A)** To test the specificity of the GLP1R antibody for use in western blots, cell lysates were collected from INS-1 and HEK293 cells, or INS-1 cells treated with either a non-targeting negative control siRNA or *Glp1r* siRNA. **(B)** Quantification of the western blots shown in **Fig. S7A**. GLP1R protein levels were normalized to GAPDH and expressed as fold change from INS-1 or control (ctrl) siRNA treated samples. N=1 per condition. **(C)** Whole blot images of the GLP1R and GAPDH western blots shown in **Figure 2D**. **(D)** INS-1 cells were transfected with 30 nM miR-192 inhibitor or a non-targeting control for 48 hours, and GLP1R protein levels normalized to GAPDH were quantified by western blot analysis. **(E)** Quantification of the western blots shown in **Fig. S7D**. GLP1R protein levels were normalized to GAPDH and expressed as fold change from non-targeting control treated samples. Statistical significance was determined by unpaired t-test, \* $p < 0.05$

**A****B****C****D**

**Supplementary Figure 8. Validation of knockdown and overexpression efficiencies for genetic manipulations in INS-1 cells.** (A, B) INS-1 cells were transfected with siRNAs targeting Ago2 (A), Tnrc6b (B), or a negative control siRNA for 48 hours, followed by transfection with a scrambled control mimic or miR-192 mimic for an additional 48 hours. Ago2 (A) and Tnrc6b (B) transcript levels were quantified by RT-qPCR and normalized to *Clptm1*. (C, D) INS-1 cells were co-transfected with expression vectors encoding human FXR1 or TNRC6B, together with a scrambled control mimic or miR-192 mimic, for 48 hours. FXR1 (C) and TNRC6B (D) transcript levels were quantified by RT-qPCR and normalized to *Clptm1*. Data are presented as mean  $\pm$  SEM. Statistical significance was determined by unpaired t-test, \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001, \*\*\*\*p < 0.0001.



**Supplementary Figure 9.** INS-1 cells were co-transfected with a human TNRC6B overexpression vector together with miR-192 mimic or scrambled control. Shown is a linear regression analysis of *Glp1r* transcript levels plotted against the ratio of *Fxr1* to *TNRC6B* transcript levels.



**Supplementary Figure 10. Effects of miR-192 on apoptosis markers in rodent  $\beta$  cell models.** INS-1, MIN6, and  $\beta$ TC3 cells were transfected with miR-192 mimic or a scrambled control for 48 hours before cells were collected for Caspase-3/7 and Annexin V (Invitrogen, #88-8006-72) quantifications according to manufacturers' instructions on an Agilent BioTek Synergy H1 plate reader.