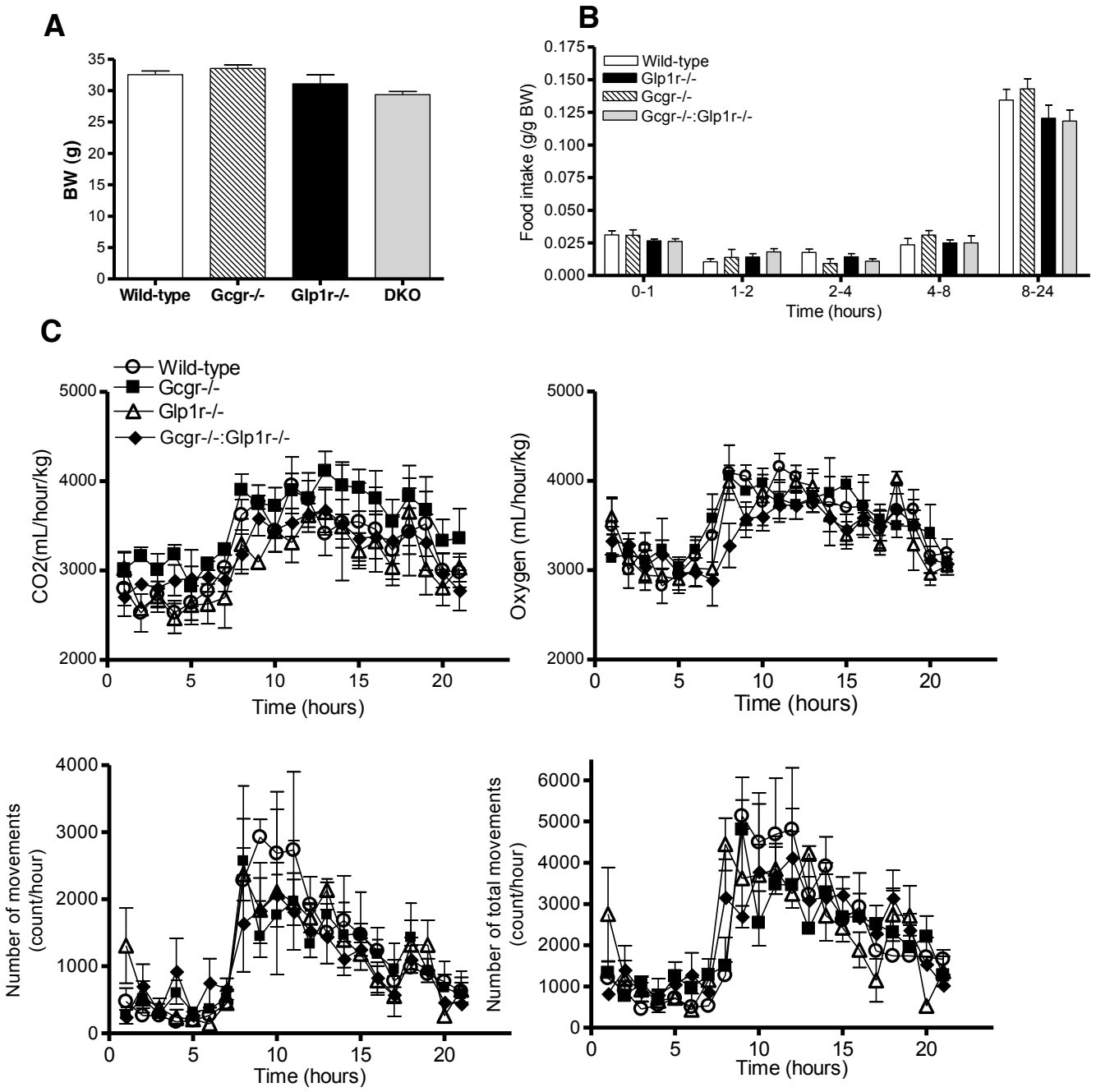
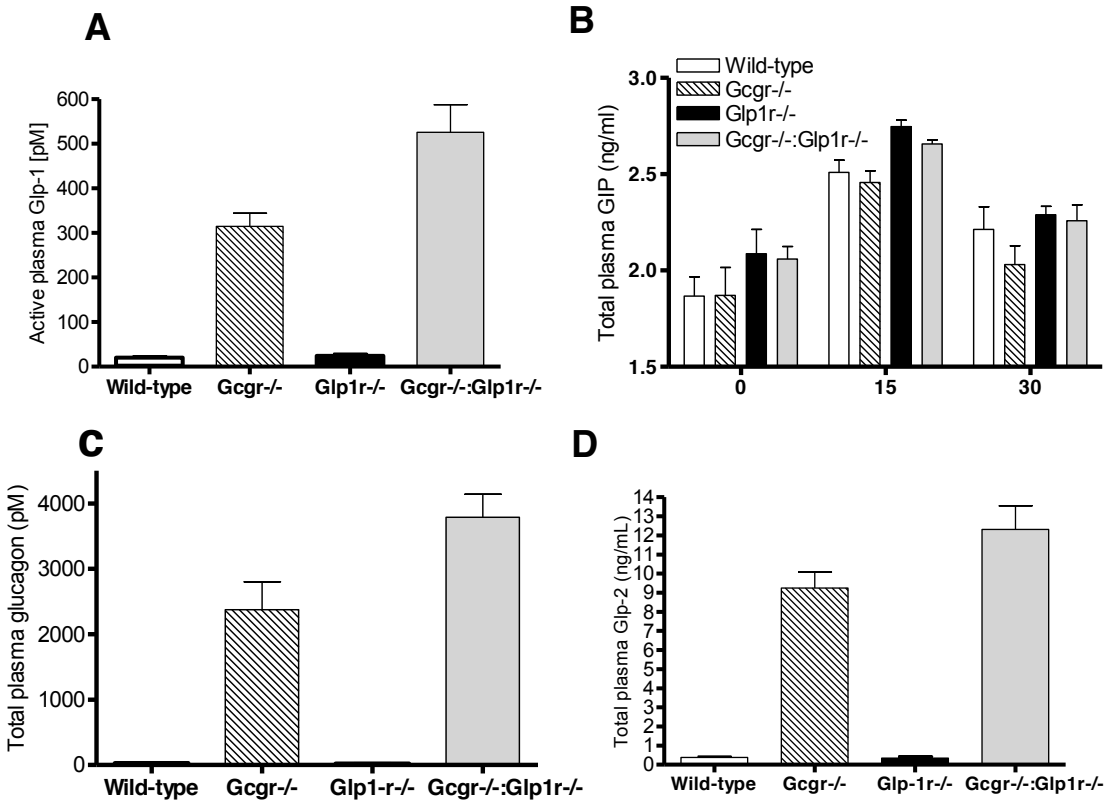
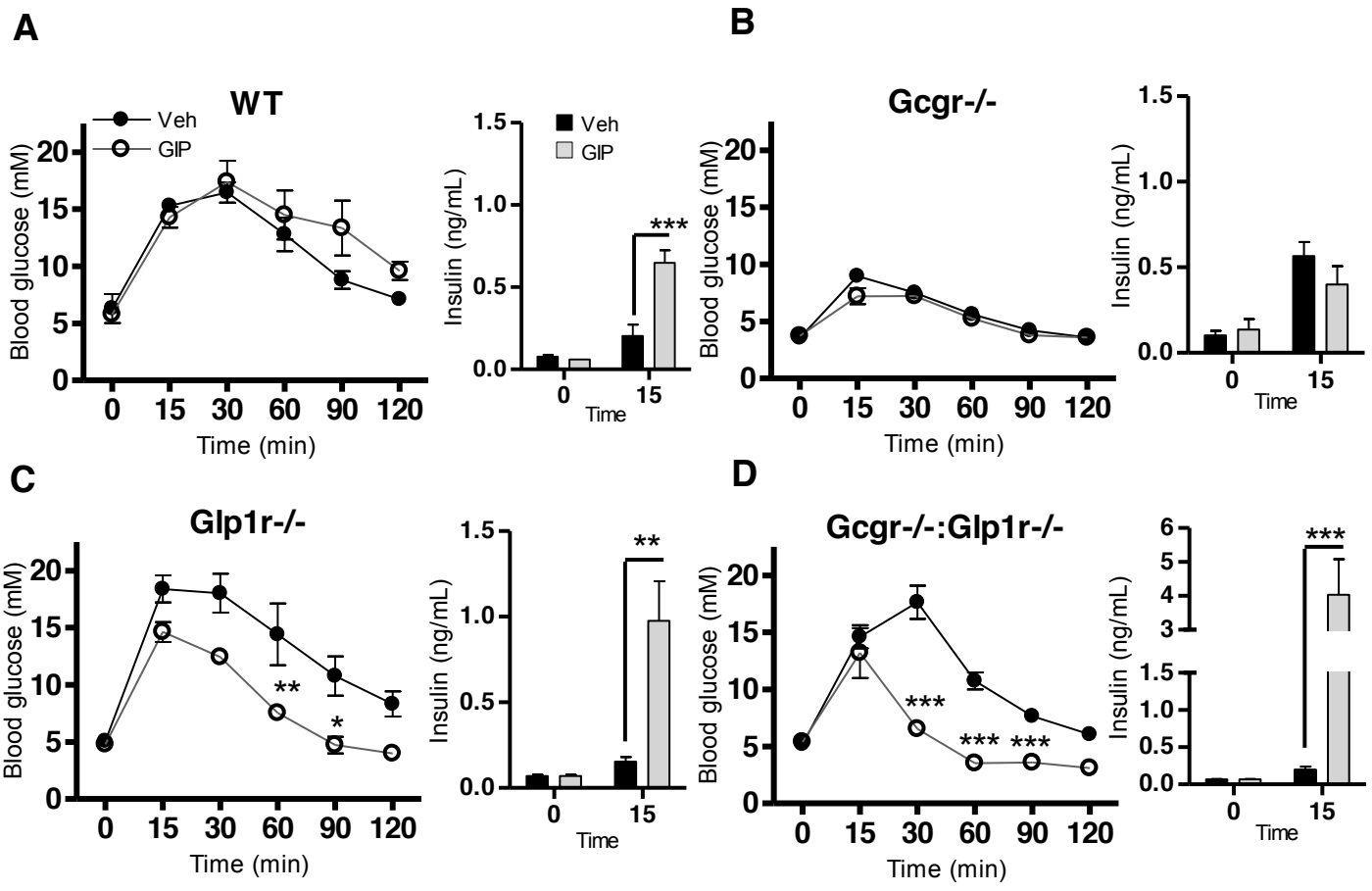


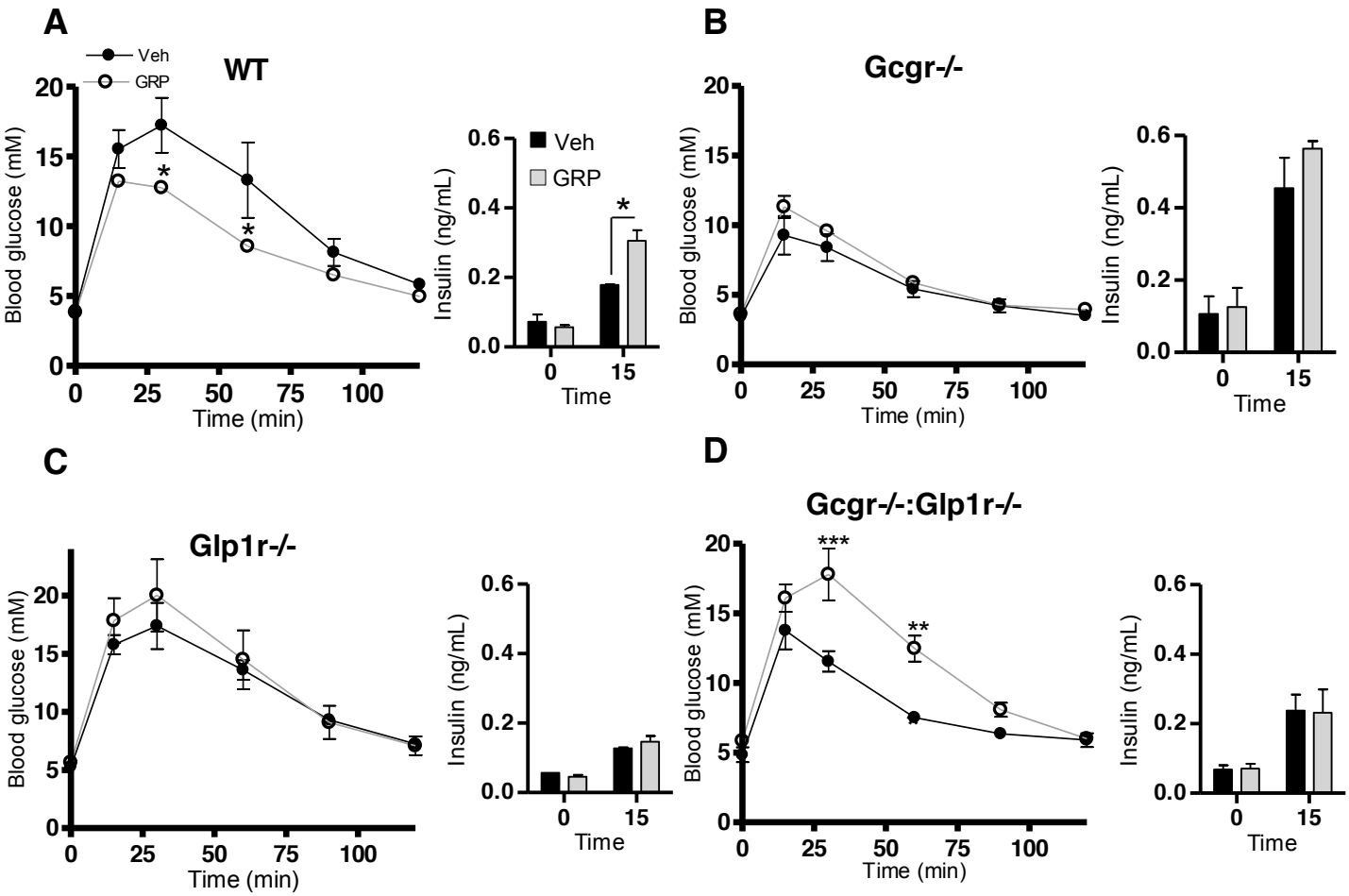
Supplementary Figure 1. Body weight, food intake and energy expenditure. (A) Body weight from 12 week old mice (n = 4-7). (B) Food intake was determined 1, 2, 4, 8 and 24 hours following an overnight fast (n = 4-16). (C) Energy expenditure was determined in 8-10 week old mice. Oxymax measurements were starting at 12pm (n = 6 mice per genotype). Values are expressed as mean ± SEM.



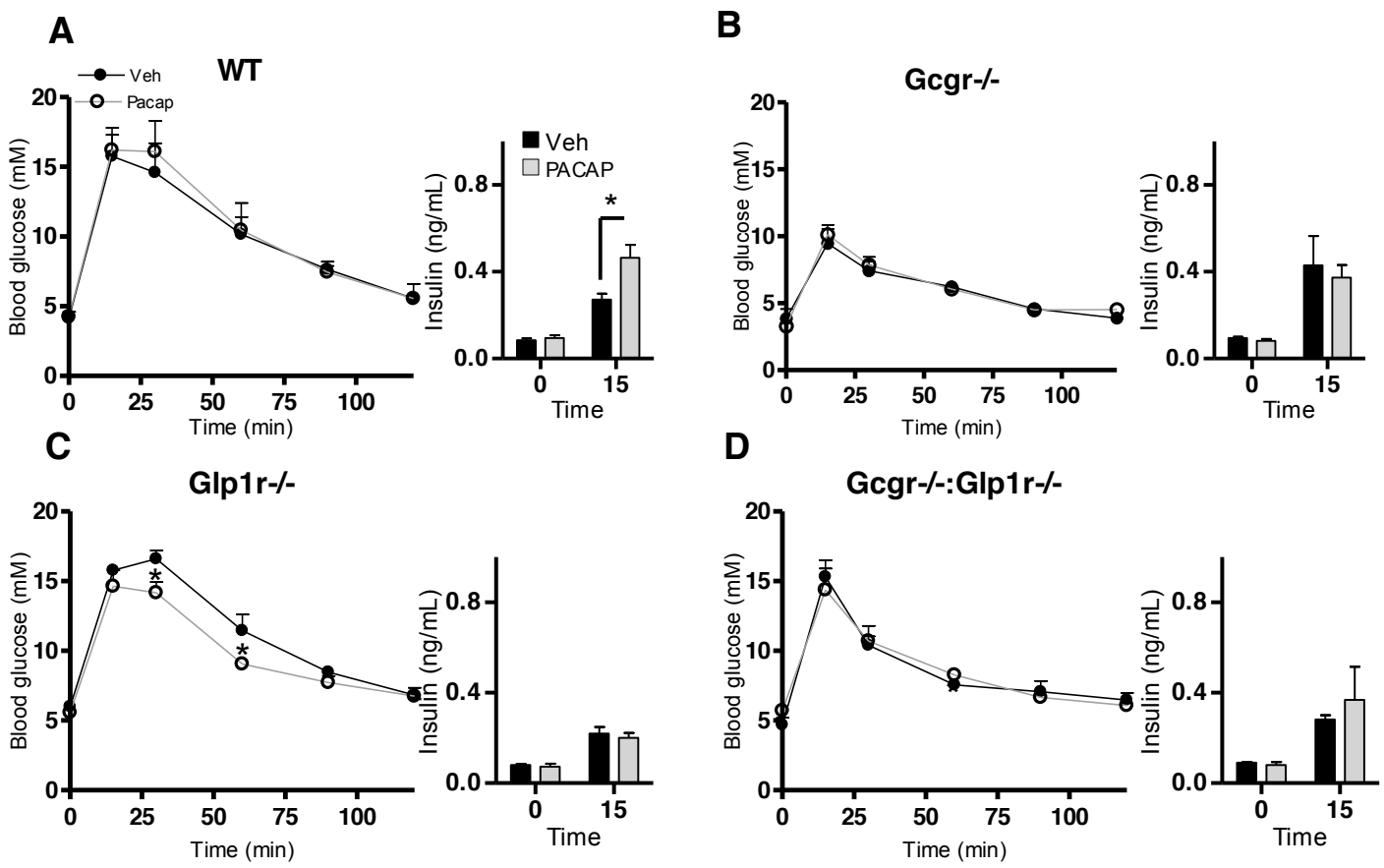
Supplementary Figure 2. ***Plasma levels of total GIP, active GLP-1, total GLP-2 and total Glucagon.*** (A) Random fed active GLP-1 levels in plasma. (B) Plasma levels of total GIP at 0, 15 and 30 min following oral glucose administration. (C) Random fed total glucagon levels in plasma. (D) Random fed total GLP-2 levels in plasma. n=4-10 per genotype. Values are expressed as mean ± SEM.



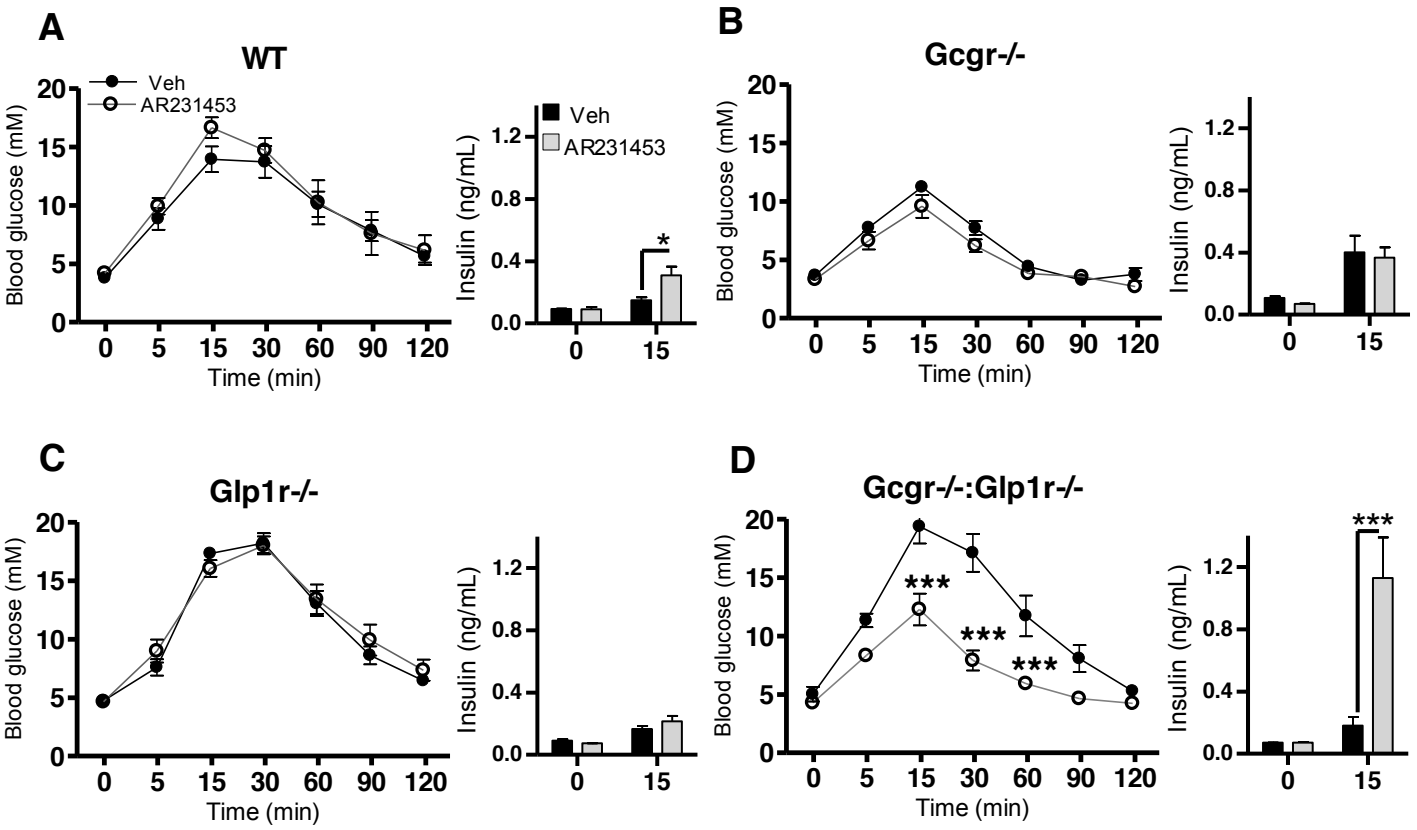
Supplementary Figure 3. ***Gcgr$^{-/-}$:Glp1r$^{-/-}$ mice exhibit enhanced sensitivity to D-Ala$_2$ GIP.*** Intraperitoneal glucose tolerance test was performed in 22-24 week old (A) WT, (B) *Gcgr$^{-/-}$,* (C) G*lp1r$^{-/-}$* ;and (D) *Gcgr$^{-/-}$*:*Glp1r$^{-/-}$* mice immediately following treatment with 2nM of D-Ala$_2$ GIP or saline. Insets depict plasma insulin levels 0 and 15 min following glucose challenge (n = 5-8). Values are expressed as mean ± SEM; **P* < 0.05, ***P <0.01*, *** *P<.001* D-Ala$_{2-}$ vs. vehicle- treated mice.



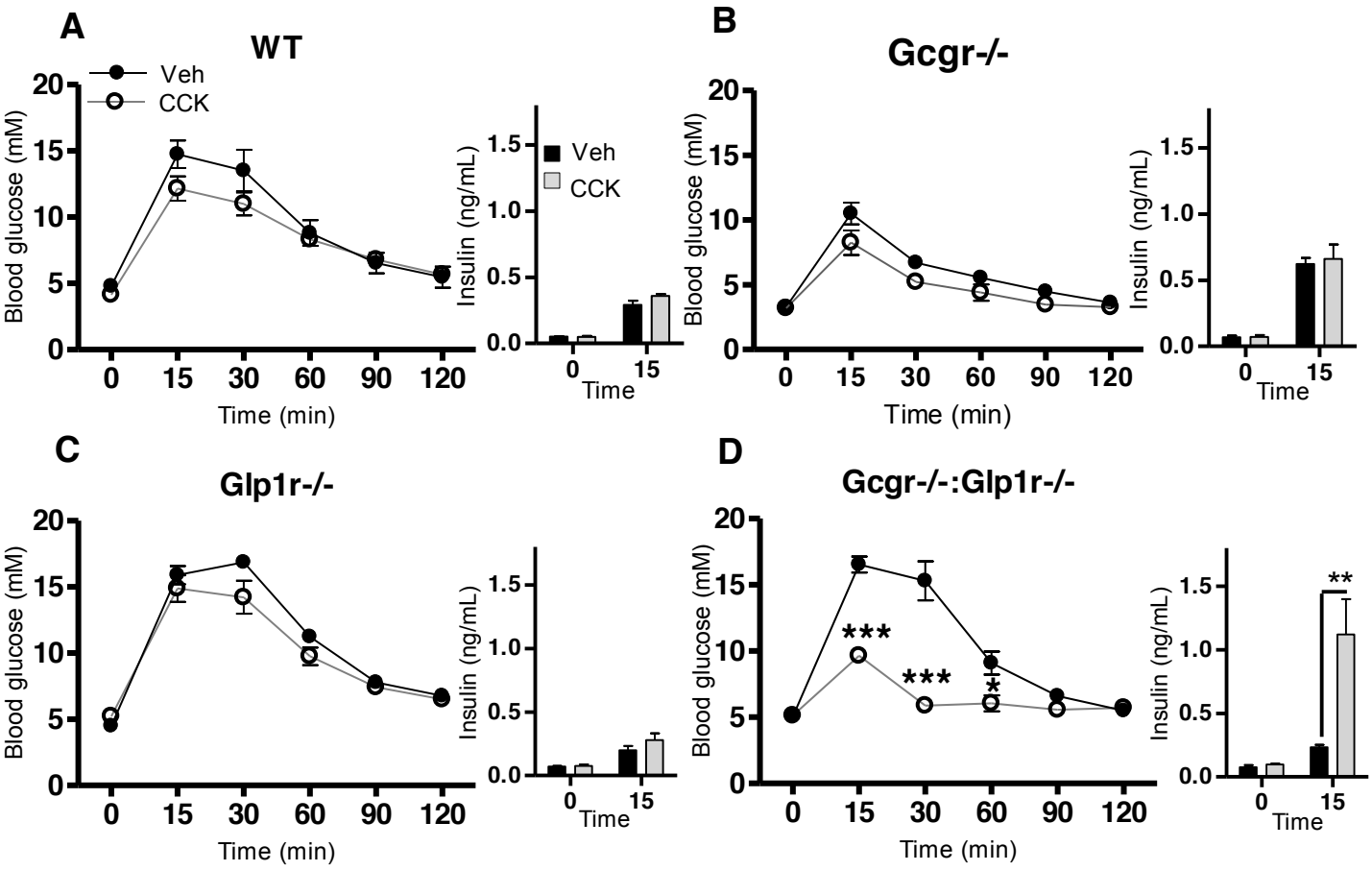
Supplementary Figure 4. ***GRP action in WT and knockout mice.*** Intraperitoneal glucose tolerance test was performed in 22-24 week old (A) WT, (B) *Gcgr*$^{-/-}$, (C) G*lp1r*$^{-/-}$;and (D) *Gcgr*$^{-/-}$:*Glp1r*$^{-/-}$ mice immediately following treatment with 20 nmol/kg of GRP or with saline. Insets depict plasma insulin levels at 0 and 15 min following glucose challenge (n = 5-8). Values are expressed as mean ± SEM; **P* < 0.05, ***P <0.01*, *** *P<.001* GRP- vs. vehicle- treated mice.



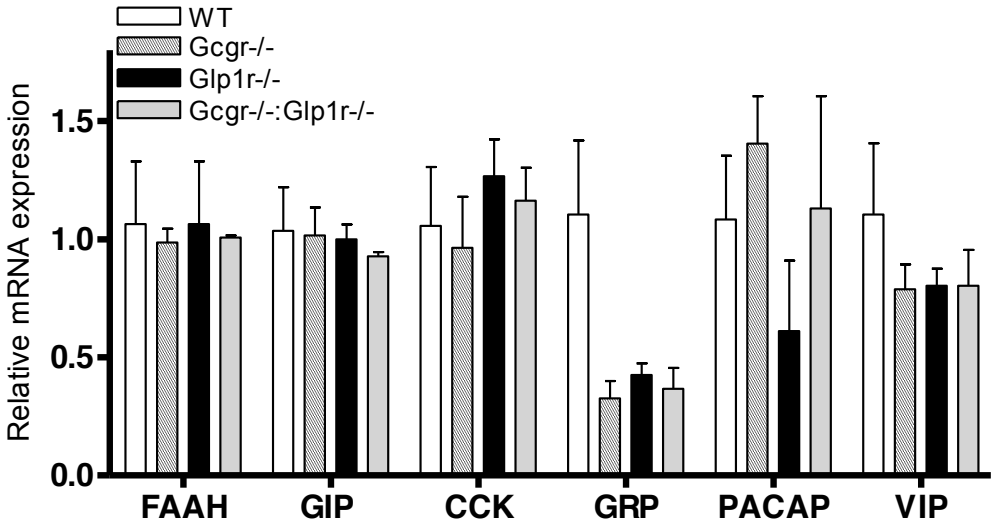
Supplementary Figure 5. ***PACAP action in WT and knockout mice.*** Intraperitoneal glucose tolerance test was performed in 22-24 week old mice A) WT, (B) *Gcgr*$^{-/-}$, (C) G*lp1r*$^{-/-}$;and (D) *Gcgr*$^{-/-}$:*Glp1r*$^{-/-}$ mice immediately following treatment with 1.3 nmol/kg of PACAP-38 or saline. Insets depict plasma insulin levels at 0 and 15 min following glucose challenge (n = 5-8). Values are expressed as mean ± SEM; **P* < 0.05 for PACAP-38- vs. vehicle- treated mice.



Supplementary Figure 6. Enhanced *sensitivity to the GPR119 agonist AR231453.* An Intraperitoneal glucose tolerance test was performed in 22-24 week old (A) WT, (B) *Gcgr*$^{-/-}$, (C) G*lp1r*$^{-/-}$;and (D) *Gcgr*$^{-/-}$:*Glp1r*$^{-/-}$ mice 30 min following treatment with 20mg/kg of AR231453 or vehicle. Insets depict plasma insulin levels at 0 and 15 min following glucose challenge (n = 5-8). Values are expressed as mean ± SEM; **P* < 0.05, ***P <0.01*, *** *P<.001* AR231453- vs. vehicle- treated mice.



Supplementary Figure 7. Enhanced *sensitivity to CCK.* Intraperitoneal glucose tolerance test was performed in 22-24 week old (A) WT, (B) *Gcgr*$^{-/-}$, (C) G*lp1r*$^{-/-}$;and (D) *Gcgr*$^{-/-}$:*Glp1r*$^{-/-}$ mice immediately following treatment with 18ug/kg of CCK-8 or saline. Insets depict plasma insulin levels at 0 and 15 min following glucose challenge (n = 5-8). Values are expressed as mean ± SEM; **P* < 0.05, ***P <0.01*, *** *P<.001* CCK-8- vs. vehicle- treated mice.



Supplementary Figure 8*. Gut peptide gene expression in re-fed mice*. Duodenums were isolated from *Gcgr-/-*:Glp1r-/-, *Gcgr-/-*, *Glp1r-/-* and WT mice following an overnight fast and refed for 1 hour followed by assessment of basal levels of transcripts encoding FAAH, GIP, CCK, GRP, PACAP and VIP. Levels of transcripts were normalized to levels for cyclophilin for each RNA sample. n = 4 mice per genotype. Values are expressed as mean ± SEM.