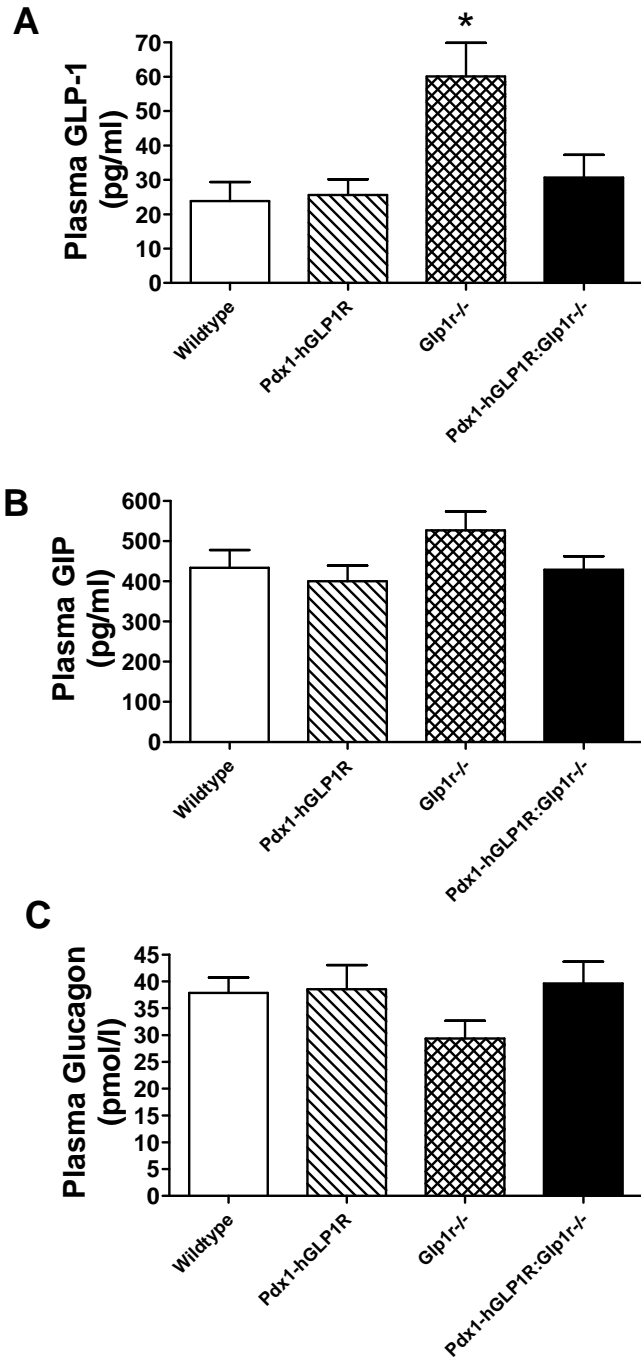
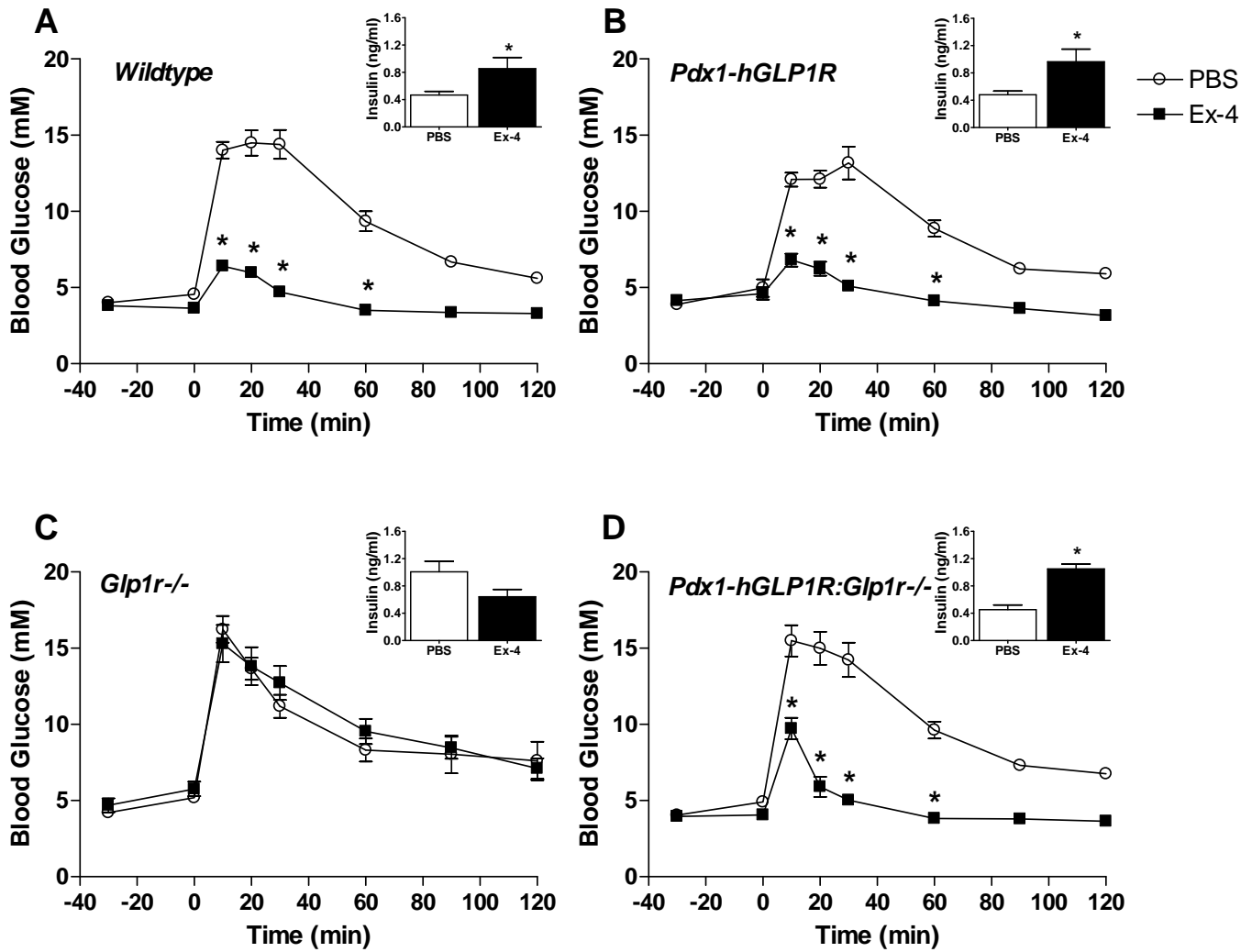


**Supplemental Figure 1.** Analysis of gene expression in islets from Pdx1-hGLP1R:Glp1r<sup>-/-</sup> and control mice. Real-time PCR analysis determined the relative levels of Pdx1, Gipr, Glut2, Gck, Kir6.2, Akt1, and Ins2 gene transcripts in islets from wild-type, Pdx1-hGLP1R, Glp1r<sup>-/-</sup> and Pdx1-hGLP1R:Glp1r<sup>-/-</sup> mice. Ppia was used as an internal control gene. n=6-8



**Supplemental Figure 2.** Plasma hormone levels in Pdx1-hGLP1R:*Glp1r*<sup>-/-</sup> and control mice following oral glucose administration. Total GLP-1 (A), total GIP (B) and glucagon (C) levels were measured in plasma collected 10 min after oral glucose administration.



**Supplemental Figure 3.** The effect of exendin-4 (Ex-4) on oral glucose tolerance is restored in Pdx1-hGLP1R:Glp1r-/- mice. The response to an oral glucose challenge (OGTT, 1.5 g/kg of body weight) in fasted male mice was assessed 30 min after an IP injection of either vehicle (PBS) or Ex-4 (1  $\mu$ g). Blood glucose levels in wildtype (A), Pdx1-hGLP1R (B), Glp1r-/- (C) and Pdx1-hGLP1R:Glp1r-/- mice (D) were monitored throughout the experiment. Plasma insulin levels (insets) were measured in samples collected 10 min after glucose administration. n=6-11, \*P<0.05 vs. PBS