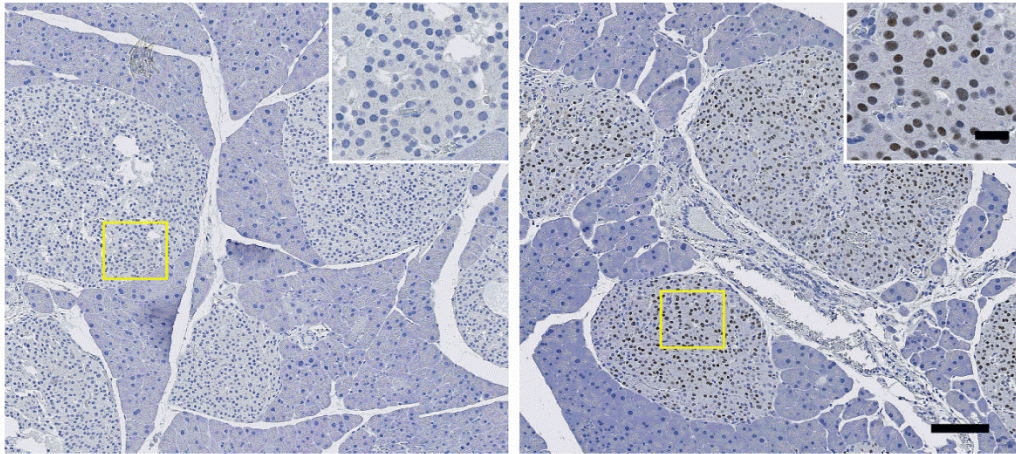
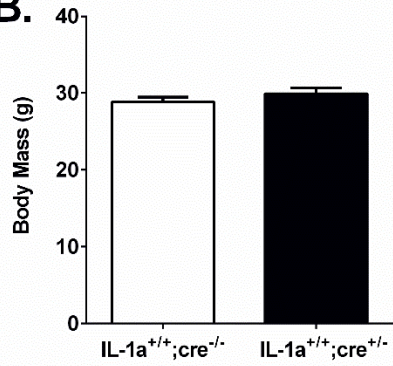
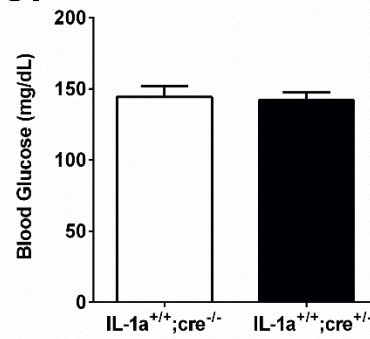
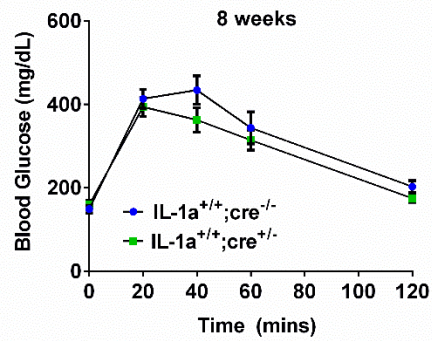
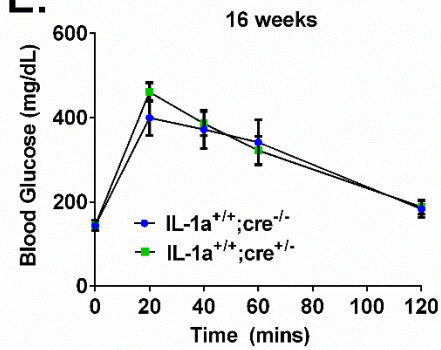
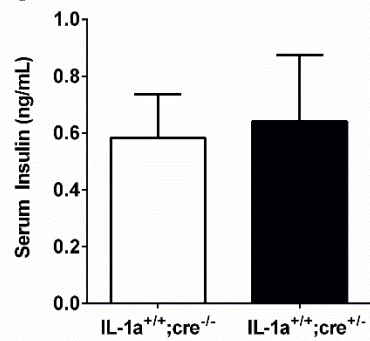
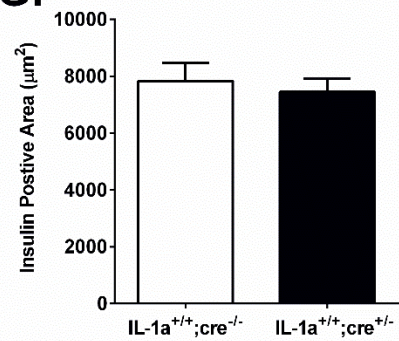
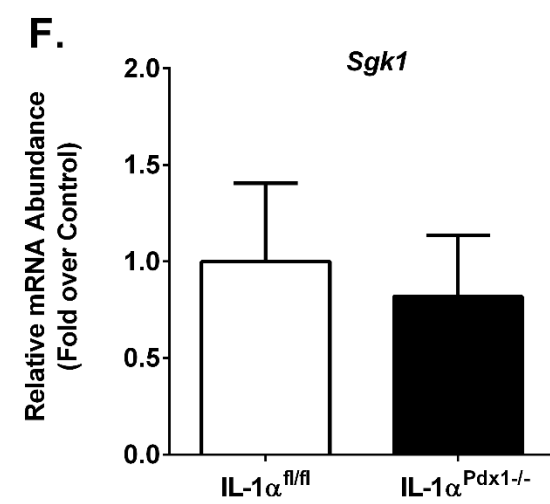
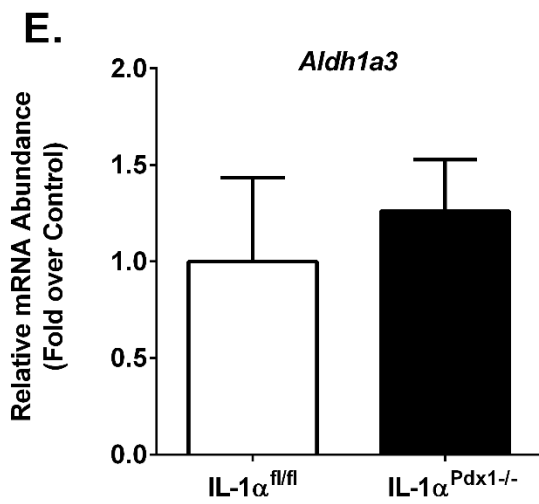
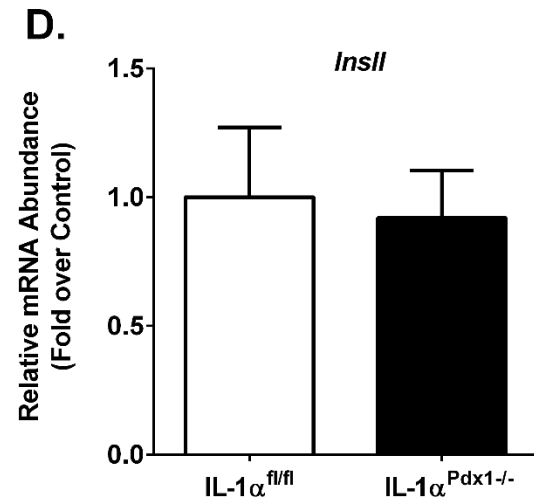
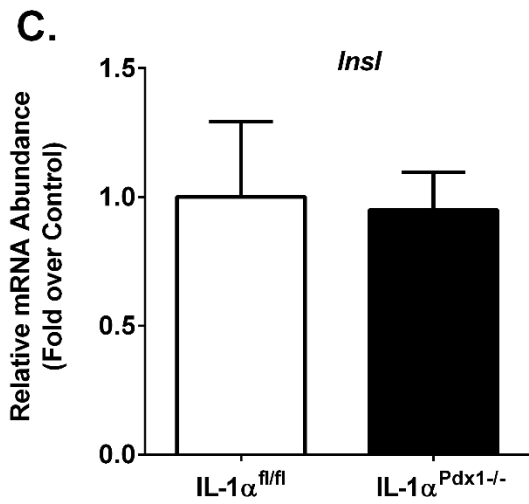
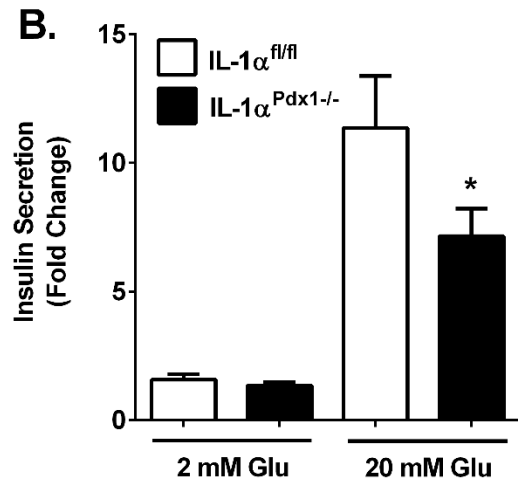
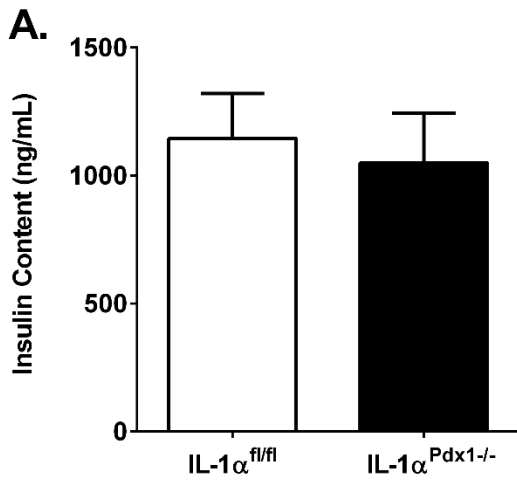


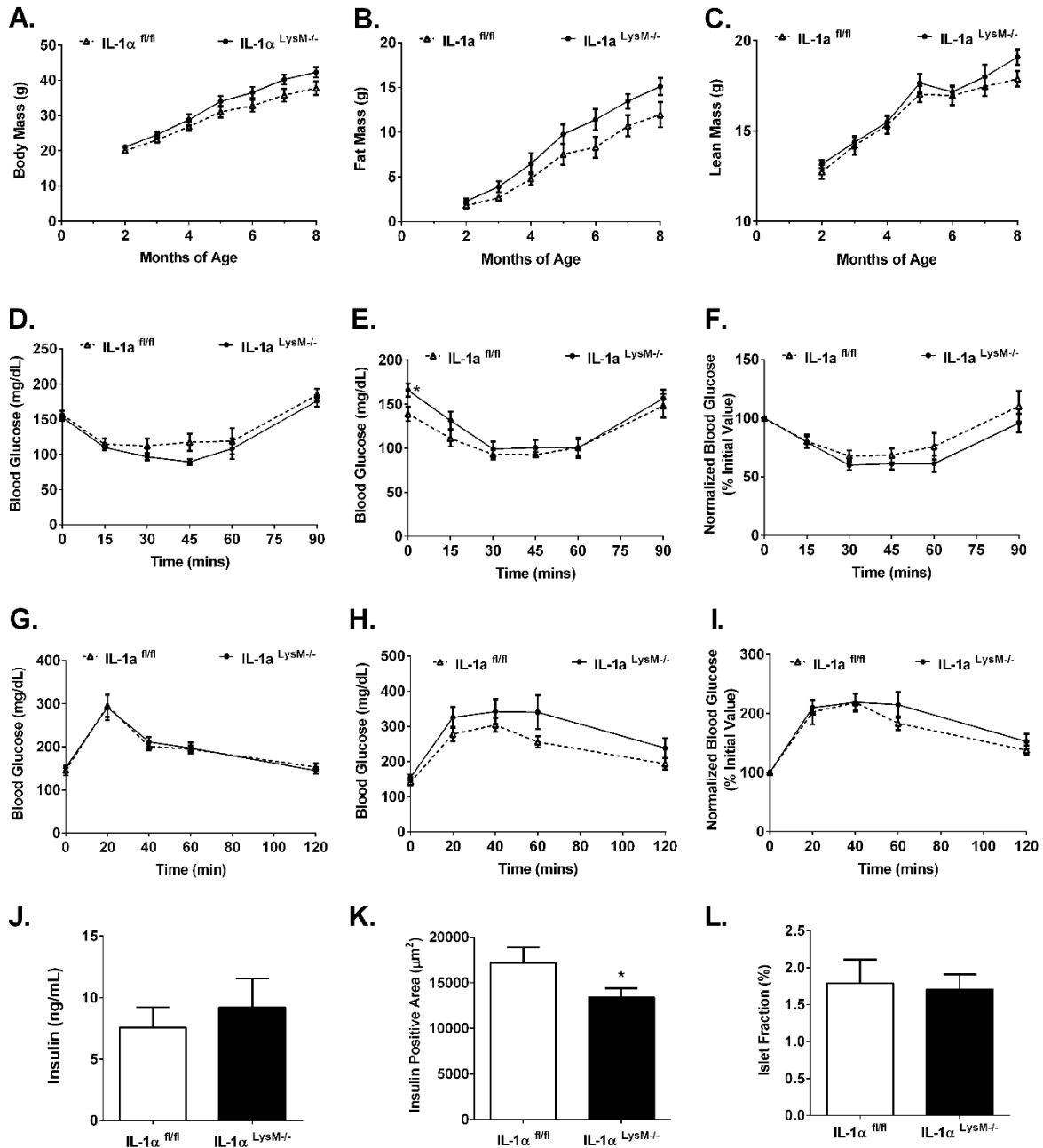
**A.****B.****C.****D.****E.****F.****G.**

**Supplementary Figure 1. Non-floxed cre-positive mice display no alterations in body mass, glucose tolerance, or insulin levels compared to control mice.** (A) cre staining in pancreatic sections of 9 month old male IL-1 $\alpha$ <sup>fl/fl</sup> (left panel) and IL-1 $\alpha$ <sup>Pdx1<sup>-/-</sup></sup> (right panel) mice. Scale bar = 100  $\mu$ m for larger image and 20  $\mu$ m for inset. Body mass (B) and fasting blood glucose levels (C) in 16 week old male IL-1 $\alpha$ <sup>+/+</sup>; cre<sup>-/-</sup> and IL-1 $\alpha$ <sup>+/+</sup>; cre<sup>+/-</sup> mice. GTTs conducted using (D) 8 week old and (E) 16 week old male IL-1 $\alpha$ <sup>+/+</sup>; cre<sup>-/-</sup> and IL-1 $\alpha$ <sup>+/+</sup>; cre<sup>+/-</sup> mice. Serum insulin (F) and insulin positive area (G) in 16 week old male IL-1 $\alpha$ <sup>+/+</sup>; cre<sup>-/-</sup> and IL-1 $\alpha$ <sup>+/+</sup>; cre<sup>+/-</sup> mice.



**Supplementary Figure 2. Pancreatic deletion of IL-1 $\alpha$  does not alter intracellular insulin content, or promote de-differentiation, but decreases glucose-stimulated insulin secretion.**

(A) Insulin content in islets of 5 month old male IL-1 $\alpha^{fl/fl}$  and IL-1 $\alpha^{Pdx1^{-/-}}$  mice. (B) Glucose-stimulated insulin secretion from islets of 5 month old male IL-1 $\alpha^{fl/fl}$  and IL-1 $\alpha^{Pdx1^{-/-}}$  mice in response to 2 mM or 20 mM glucose. (C-F). qPCR analysis of transcript levels of the *InsI* (C), *InsII* (D), *Aldh1a3* (E), and *Sgk1* (F) genes in islets from 5 month old male IL-1 $\alpha^{fl/fl}$  and IL-1 $\alpha^{Pdx1^{-/-}}$  mice. (A-B) n = 7-9 per group; (C-D) n= 6-7 per group. \*,  $p < 0.05$  vs. IL-1 $\alpha^{fl/fl}$  control at 20 mM glucose. Glu = glucose.



**Supplementary Figure 3. Deletion of IL-1 $\alpha$  in myeloid cells has no impact on body composition, whole body glucose tolerance, or insulin sensitivity, in female mice.** (A) Body mass, (B) fat mass, and (C) lean mass in female IL-1 $\alpha$ <sup>fl/fl</sup> and IL-1 $\alpha$ <sup>LysM<sup>-/-</sup></sup> mice from 2- 8 months of age. (D-F) Insulin tolerance tests (ITT) performed in (D) 3 month and (E) 7 month old female

IL-1 $\alpha$ <sup>fl/fl</sup> and IL-1 $\alpha$ <sup>LysM<sup>-/-</sup></sup> mice. (F) ITT data from panel E. expressed as a percentage of the initial (i.e., pre-glucose i.p.) value. (G-I) Glucose tolerance tests (GTT) conducted in (G) 4 month and (H) 8 month old female IL-1 $\alpha$ <sup>fl/fl</sup> and IL-1 $\alpha$ <sup>LysM<sup>-/-</sup></sup> mice. (I) GTT data from panel H. expressed as a percentage of the initial (i.e., pre-glucose i.p.) value. (J) Serum insulin, (K) insulin positive area, and (L) islet fraction from 9 month old female IL-1 $\alpha$ <sup>fl/fl</sup> and IL-1 $\alpha$ <sup>LysM<sup>-/-</sup></sup> mice. n = 7-8 per group.

\*  
,  $p < 0.05$ .