#### **EXTENDED METHODS**

#### Statistics.

N numbers for Figure 1: (B) controls = 20; GLP1R KD<sup> $\Delta$ Nestin</sup> = 6; GLP1R KD<sup> $\Delta$ Phox2b</sup> = 5. (C) controls = 20, GLP1R KD<sup> $\Delta$ Nestin</sup> = 16, GLP1R KD<sup> $\Delta$ Phox2b</sup> = 22. (D) controls = 20, GLP1R KD<sup> $\Delta$ Nestin</sup> = 16, GLP1R KD<sup> $\Delta$ Phox2b</sup> = 20. (E) controls = 20, GLP1R KD<sup> $\Delta$ Nestin</sup> = 15, GLP1R KD<sup> $\Delta$ Phox2b</sup> = 20. (F) controls = 19, GLP1R KD<sup> $\Delta$ Nestin</sup> = 12, GLP1R KD<sup> $\Delta$ Phox2b</sup> = 17.

N numbers for Figure 2: (A-B) each treatment had controls = 20, GLP1R KD<sup> $\Delta$ Nestin</sup> = 6, GLP1R KD<sup> $\Delta$ Phox2b</sup> = 5. (C-D) each saline-treated group = 8, each liraglutide-treated group = 7. (E) saline-treated controls = 16, liraglutide-treated controls = 15, lithium chloride treated controls = 11, saline-treated GLP1R KD<sup> $\Delta$ Nestin</sup> = 6, liraglutide-treated GLP1R KD<sup> $\Delta$ Nestin</sup> = 7, lithium chloride-treated GLP1R KD<sup> $\Delta$ Nestin</sup> = 5, saline-treated GLP1R KD<sup>Phox2b</sup> = 9, liraglutide-treated GLP1R KD<sup>Phox2b</sup> = 9, lithium chloride-treated GLP1R KD<sup>Phox2b</sup> = 8.

N numbers for Figure 3: saline-treated controls = 10, saline-treated GLP1R KD<sup> $\Delta$ Nestin</sup> = 7, saline-treated GLP1R KD<sup> $\Delta$ Phox2b</sup> = 11, liraglutide-treated controls = 10, liraglutide-treated GLP1R KD<sup> $\Delta$ Nestin</sup> = 8, liraglutide-treated GLP1R KD<sup> $\Delta$ Phox2b</sup> = 9.

N numbers for Figure 4: (A-B) controls = 9, GLP1R KD<sup> $\Delta$ Nestin</sup> = 8, GLP1R KD<sup> $\Delta$ Phox2b</sup> =9. (C-D) controls = 14, GLP1R KD<sup> $\Delta$ Nestin</sup> = 14. (E-F) controls = 10, GLP1R KD<sup> $\Delta$ Nestin</sup> = 7, GLP1R KD<sup> $\Delta$ Phox2b</sup> = 11. (G) controls = 5, GLP1R KD<sup> $\Delta$ Nestin</sup> = 5, GLP1R KD<sup> $\Delta$ Phox2b</sup> = 5. (H-I) controls = 10, GLP1R KD<sup> $\Delta$ Nestin</sup> = 8, GLP1R KD<sup> $\Delta$ Phox2b</sup> = 10.

N numbers for Figure 5: (A) liraglutide-treated controls = 9, liraglutide-treated GLP1R KD<sup> $\Delta$ Nestin</sup> = 8, liraglutide-treated GLP1R KD<sup> $\Delta$ Phox2b</sup> = 12. (B) liraglutide-treated controls = 10, liraglutide-treated GLP1R KD<sup> $\Delta$ Nestin</sup> = 8, liraglutide-treated GLP1R KD<sup> $\Delta$ Phox2b</sup> = 9. (C) liraglutide-treated controls = 5, liraglutide-treated GLP1R KD<sup> $\Delta$ Nestin</sup> = 5, liraglutide-treated GLP1R KD<sup> $\Delta$ Phox2b</sup> = 5. N

N numbers for Supplemental Figure 1: (A) hypothalamus, brainstem, pancreas, and lung tissues: GLP1R KD<sup> $\Delta$ Nestin</sup> = 7 controls = 11; nodose = 5/grp. (B) hypothalamus, brainstem, and nodose tissues: GLP1R KD<sup> $\Delta$ Phox2b</sup> = 11, controls = 6; pancreas and lung tissues: controls = 8, GLP1R KD $\Delta$ <sup>Phox2b</sup>.

N numbers for Supplemental Figure 2: (A) controls = 20, GLP1R KD<sup> $\Delta$ Nestin</sup> = 7, GLP1R KD<sup> $\Delta$ Phox2b</sup> = 10. (B) controls = 12, GLP1R KD<sup> $\Delta$ Nestin</sup> = 8, GLP1R KD<sup> $\Delta$ Phox2b</sup> = 10.

N numbers for Supplemental Figure 3: saline-treated GLP-1R f/f Nestin-Cre -/- = 7, salinetreated GLP-1R f/- Nestin-Cre +/+ = 7, saline-treated GLP-1R f/f Phox2b-Cre -/- = 10, salinetreated GLP-1R f/- Phox2b-Cre +/+ = 10, liraglutide-treated GLP-1R f/f Nestin-Cre -/- = 7, liraglutide-treated GLP-1R f/- Nestin-Cre +/+ = 7, liraglutide-treated GLP-1R f/f Phox2b-Cre -/- = 10, liraglutide-treated GLP-1R f/- Phox2b-Cre +/+ = 10.



## **Supplemental Figure 1**

Validation of GLP1R KD<sup> $\Delta$ Nestin</sup> and KD<sup> $\Delta$ Phox2b</sup> mice. A. GLP1R expression in GLP1R KD<sup> $\Delta$ Nestin</sup> B. GLP-1R expression in GLP1R KD<sup> $\Delta$ Phox2b</sup> mice. Statistical analysis: two-tailed t-test. \* p < 0.05. For all graphs, black = controls, red = GLP1R KD<sup> $\Delta$ Nestin</sup>, gray = GLP1R KD<sup> $\Delta$ Phox2b</sup>.



### **Supplemental Figure 2**

Disparate food intake among GLP1R KDANestin animals. In different cohorts of animals, control and GLP1R  $KD^{\Delta Phox2b}$  animals showed no differences in chow food intake. However, GLP1R KD<sup>ΔNestin</sup> animals show similar (A) and increased (B) cumulative 24 hour food intakes compared to controls. Statistical analysis: 1-way ANOVA with Tukey post-hoc. \* p<0.05 vs. control; # p<0.05 vs. GLP1R KD $\Delta^{Phox2b}$ .



# **Supplemental Figure 3**

Food Intake response to liraglutide in different control mice. Statistical analyses: repeated measures two-way ANOVA. Main effect of drug p < 0.0001.