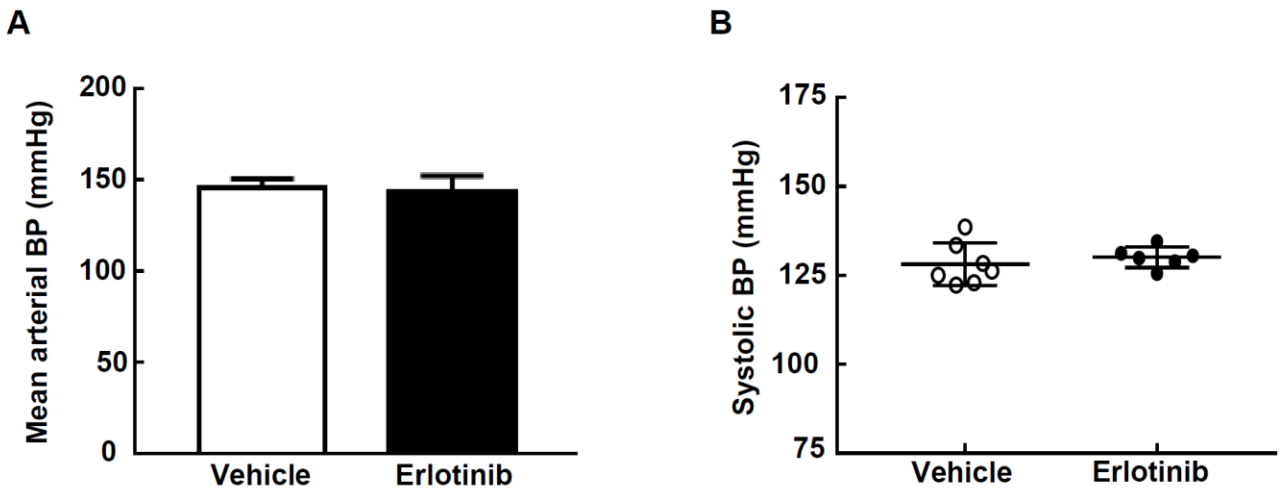
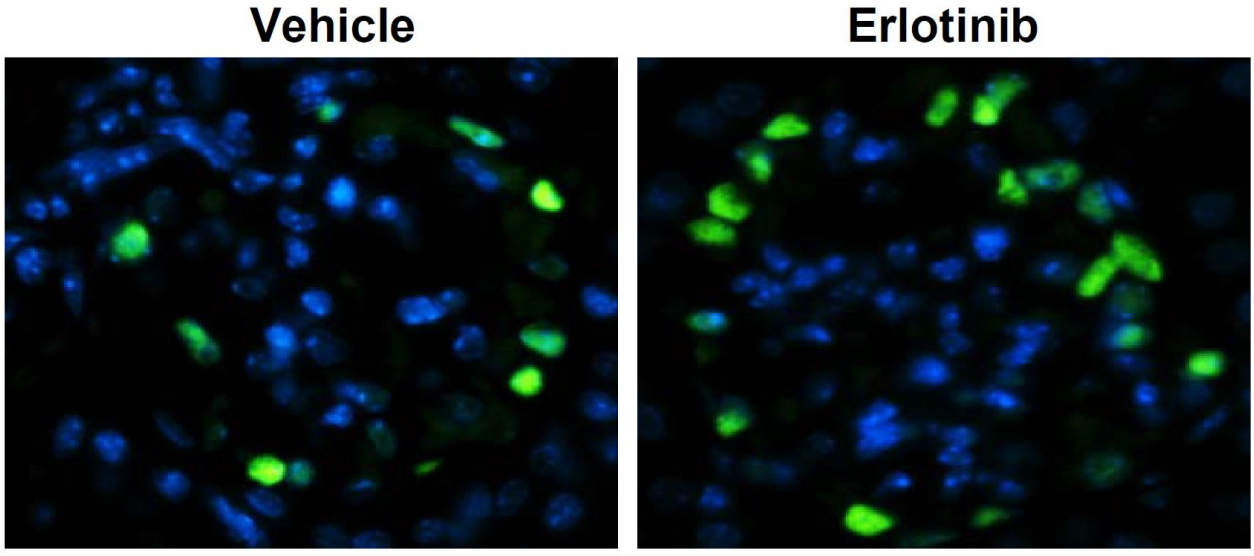
SUPPLEMENTARY DATA

Supplementary Figure S1. Erlotinib treatment had no effect on blood pressure. **A**: Erlotinib treatment of eNOS$^{-/-}$*db/db* mice from 8 to 20 weeks had no effect on blood pressure as determined by carotid catheterization. N = 6 in vehicle group and n = 4 in erlotinib group. **B**: Erlotinib treatment from 8 to 20 weeks had no effect on blood pressure as determined by tail-cuff method. N = 7 in vehicle group and n = 11 in erlotinib group.

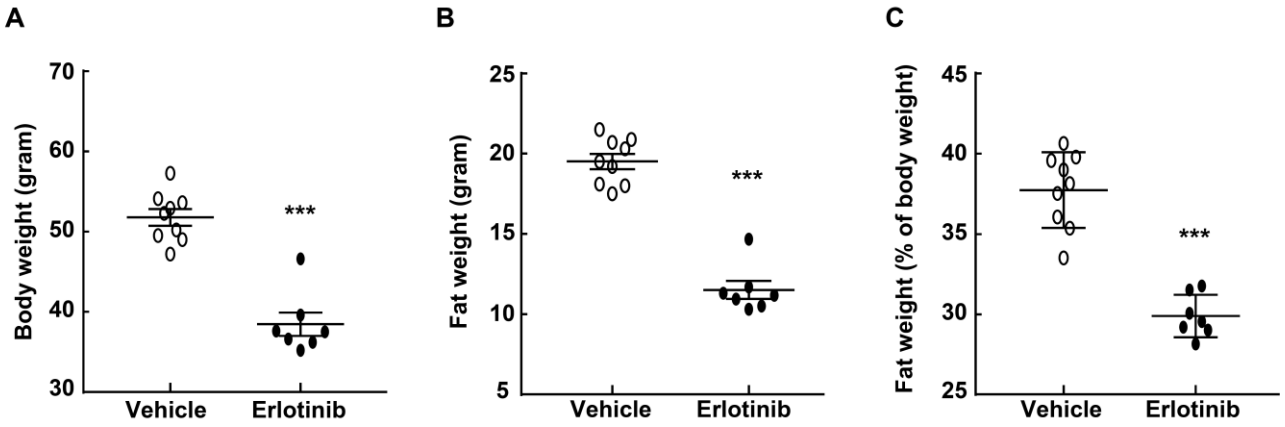


Supplementary Figure S2. Erlotinib treatment slowed podocyte loss in eNOS$^{-/-}$*db/db* mice. Erlotinib treatment from 8 to 20 weeks decreased podocyte loss as indicated by immunofluorescent staining of WT1, a marker of podocyte nucleus. Original magnification: x 400.

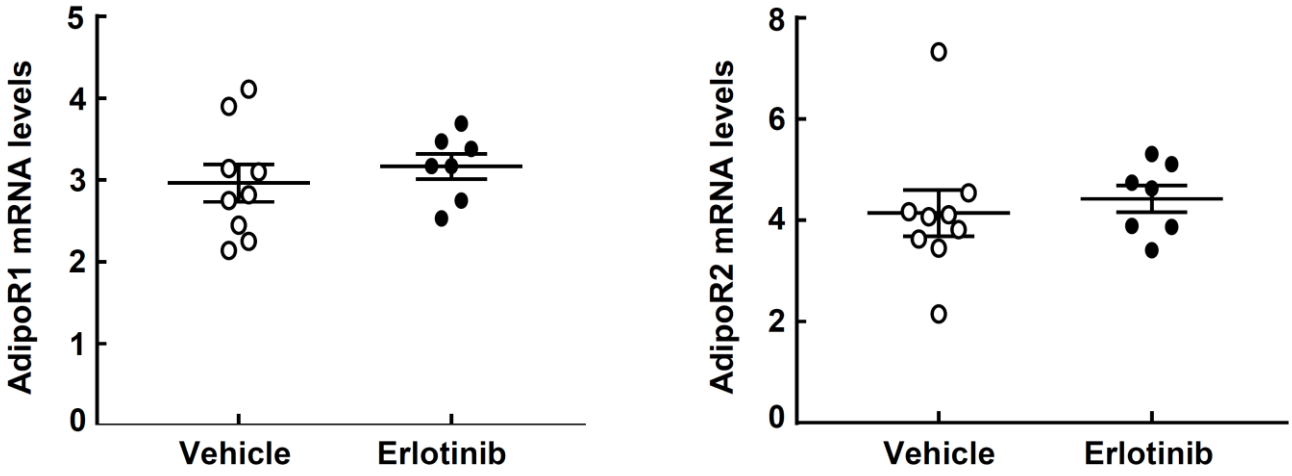


SUPPLEMENTARY DATA

Supplementary Figure S3. Erlotinib treatment decreased gains of fat tissue mass in eNOS$^{-/-}$ *db/db* mice. Erlotinib treatment from 8 to 20 weeks of age in eNOS$^{-/-}$*db/db* led to decreases in body weight (**A**), fat tissue weight (**B**), and resultant ratio of fat tissue weight vs. body weight (**C**). ***P< 0.001; n = 9 in vehicle group and n = 7 in erlotinib group.



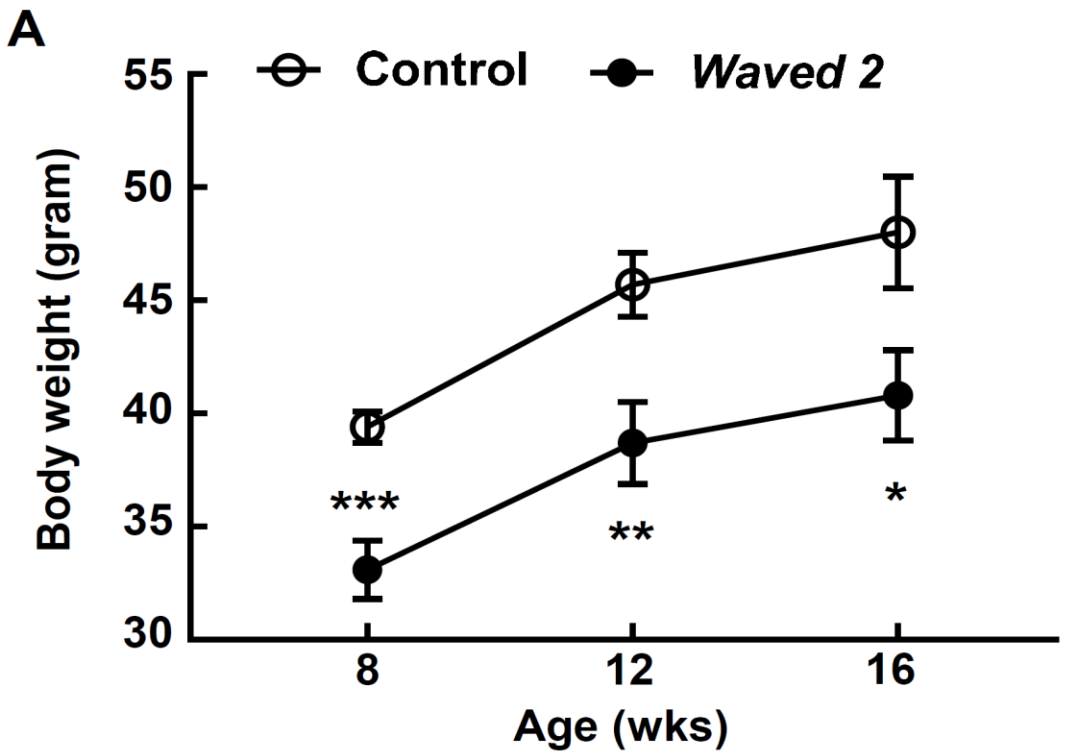
Supplementary Figure S4. Erlotinib treatment had no effect on renal adiponectin receptor expression in eNOS$^{-/-}$*db/db* mice. Erlotinib treatment from 8 to 20 weeks of age in eNOS$^{-/-}$*db/db* had no effect on renal mRNA levels of both adiponectin receptor-1 (adipoR1) and -2(adipoR2). N = 9 in vehicle group and n = 7 in erlotinib group.

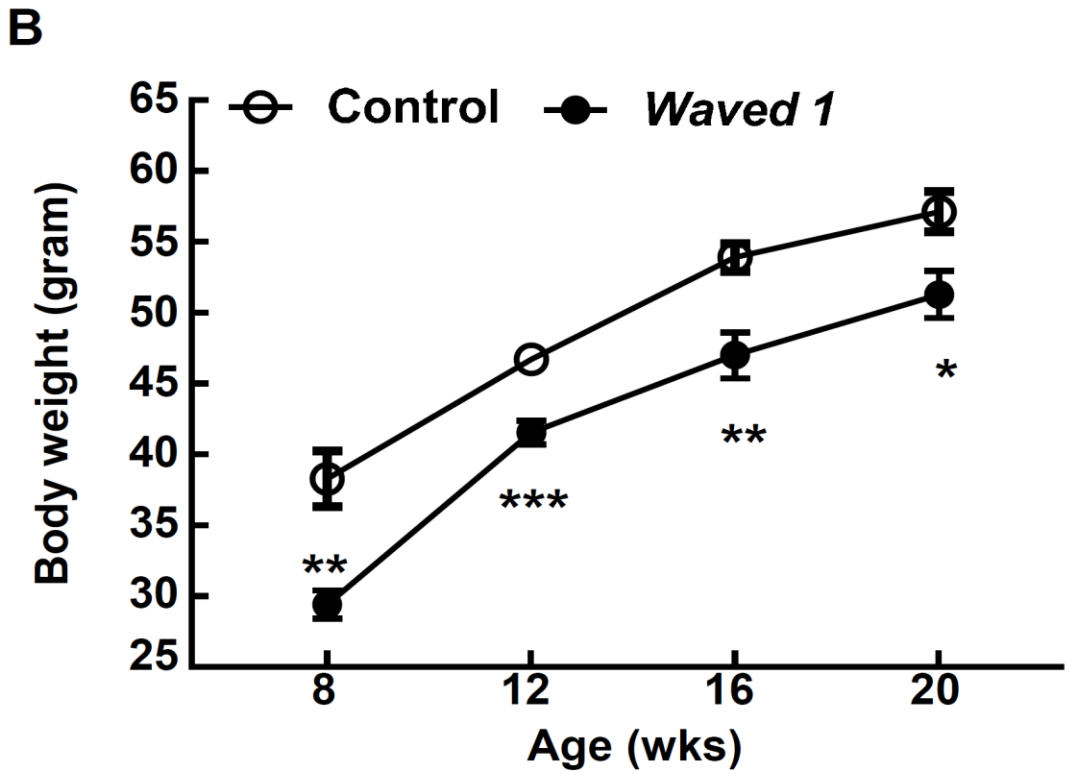


SUPPLEMENTARY DATA

Supplementary Figure S5. Genetic inhibition of EGFR signaling pathway decreased the gain of body weight in eNOS$^{-/-}$*db/db* mice. **A:***Waved 2* eNOS$^{-/-}$*db/db* mice with EGFR tyrosine kinase deficiency had less gain of body weight from 8 to 16 weeks of age. **P*< 0.05, ***P*< 0.01, ****P*< 0.001; n = 16 in each group. **B**: *Waved 1* eNOS$^{-/-}$*db/db* mice with null TGFα showed less gain of body weight from 8 to 20 weeks of age. **P*< 0.05, ***P*< 0.01, ****P*< 0.001; n = 7 in wild type group and n = 15 in *waved 1* group.

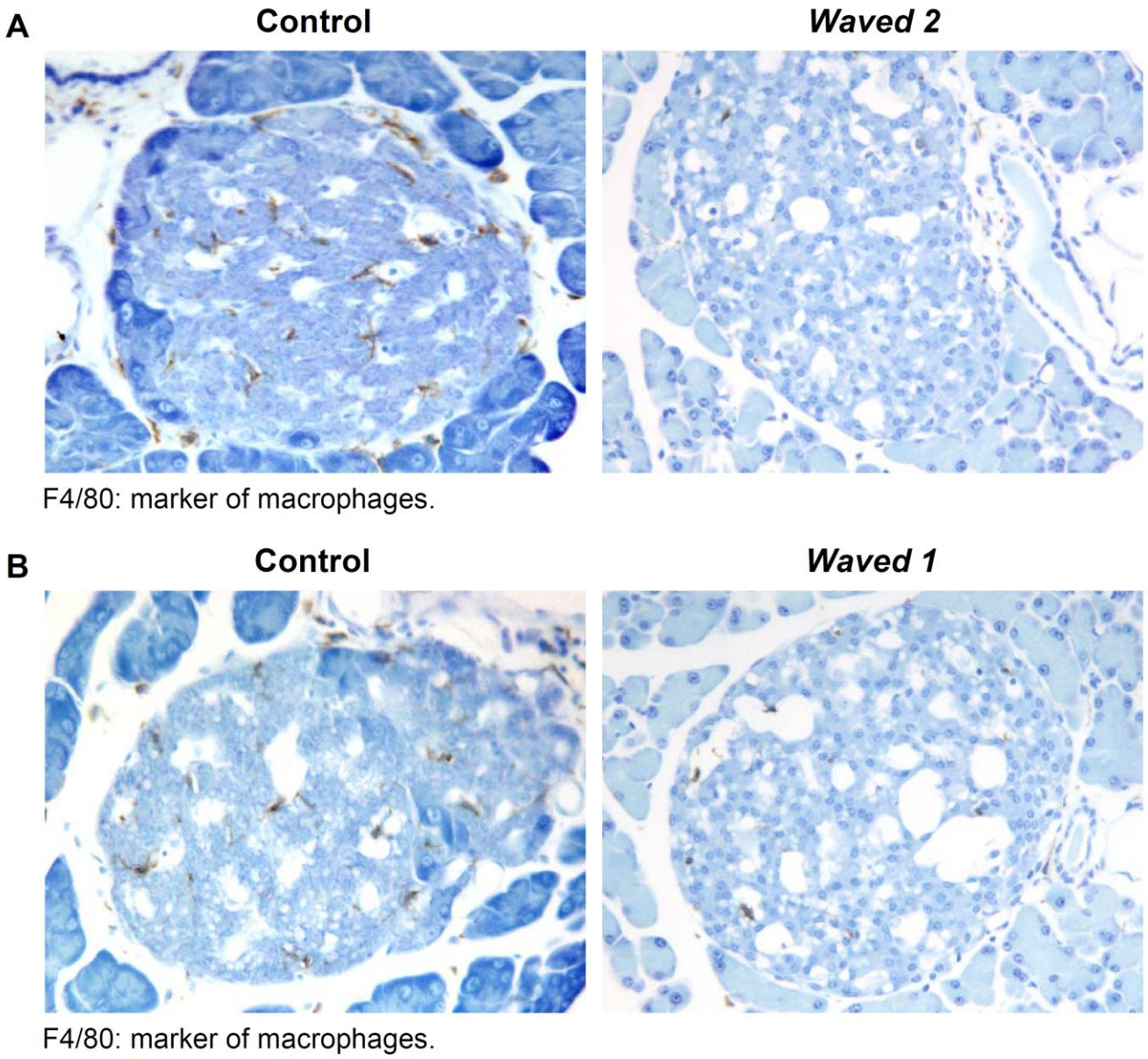
SUPPLEMENTARY DATA





SUPPLEMENTARY DATA

Supplementary Figure S6. Genetic inhibition of EGFR signaling pathway decreased islet macrophage infiltration. Both *waved 2* eNOS$^{-/-}$*db/db* mice with EGFR tyrosine kinase deficiency (**A**) and *waved 1* eNOS$^{-/-}$*db/db* mice with null TGFα(**B**) exhibited less islet macrophage infiltration, as indicated by F4/80 staining, a marker of macrophages. Original magnification: x 250.



SUPPLEMENTARY DATA

Supplementary Figure S7. *Waved 2* eNOS$^{-/-}$*db/db*mice with EGFR tyrosine kinase deficiency had similar blood pressure tocorresponding controls as determined by tail-cuff method. N = 7 in control group and n = 11 in *waved 2* group.