Online Supplemental Figure 3.
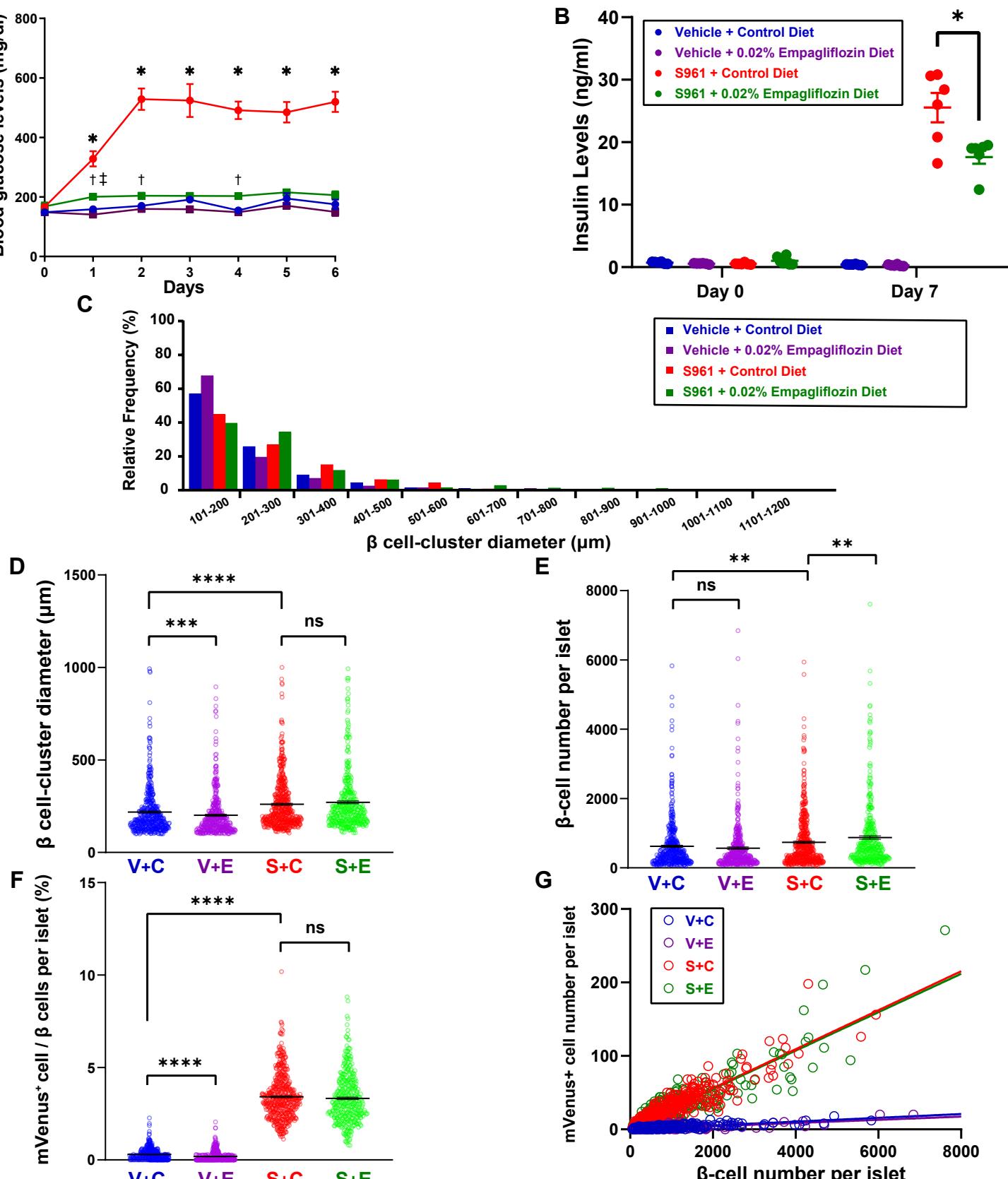

Figure S3. S961-induced β-cell proliferation is not mediated by hyperglycemia. (A, B) RIP-Cre;Fucci2aR mice were divided into four groups: 1) vehicle + control, treated with vehicle and fed control diet (N = 6); 2) vehicle + 0.02% empagliflozin, treated with vehicle and fed a diet supplemented with 0.02% empagliflozin (N = 6); 3) S961 + control, treated with S961 (10 nmol/week) and fed control diet (N = 6); and 4) S961 + 0.02% empagliflozin, treated with S961 (10 nmol/week) and fed a diet supplemented with 0.02% empagliflozin (N = 6). (A) Arbitrary blood glucose levels. *P < 0.05, S961 + control diet group vs. S961 + 0.02% empagliflozin group. †P < 0.05, S961 + 0.02% empagliflozin group vs. vehicle + control group. ‡P < 0.05, vehicle + control group vs. vehicle + 0.02% empagliflozin group. (B) Serum insulin levels at the end of the 7-day treatment. *P < 0.05, S961 + control group vs. S961 + 0.02% empagliflozin group. (C) Histogram of β-cell cluster diameter. Morphometric analysis was performed on islets harboring β-cell clusters contih diameter > 100 μm (vehicle + control, N = 4 mice, n = 496 islets; vehicle + 0.02% empagliflozin, N = 4 mice, n = 440 islets; S961 + control, N = 4 mice, n = 544 islets; S961 + 0.02% empagliflozin, N = 4 mice, n = 391 islets). (D) β-Cell cluster diameter, (E) number of β-cells per islet, and (F) percentage of mVenus+ cells per islet. **P < 0.01 (N = 4), ***P < 0.001 (N = 4), ****P < 0.0001 (N = 4);ns, not significant. (G) Correlation between number of mVenus+ cells and number of β-cells per islet. mVenus+ cell and β-cell number per islet were strongly correlated in all groups (vehicle + control, r = 0.70, P < 0.0001; vehicle + 0.02% empagliflozin diet, r = 0.61, P < 0.0001; S961 + control diet, r = 0.93, P < 0.0001; and S961 + 0.02% empagliflozin diet,r = 0.88, P < 0.0001). V + C, vehicle + control; V + E, vehicle + 0.02% empagliflozin diet; S + C, S961 + control diet; S + E, S961 + 0.02% empagliflozin diet.Data are presented as mean ± SEM.