**Supplemental Figure S1.** Both OgtHET[Endo] and OgtKO[Endo] are normal at birth. Body weight (**A**, n = 5–24), pancreas weight (**B**, n = 5–24), non-fasting blood glucose (**C**, n = 5–17), β-cell mass (**D**, n = 3–8), and α-cell mass (**E**, n = 3–8) at p0. Representative image showing normal endocrine and exocrine pancreas morphology at p0 (**F**, 10×, scale bar = 100 μm). For all graphs, open circle = Control, closed circle = OgtKO[Endo], and half-filled circle = OgtHET[Endo]. Both male and female data combined.
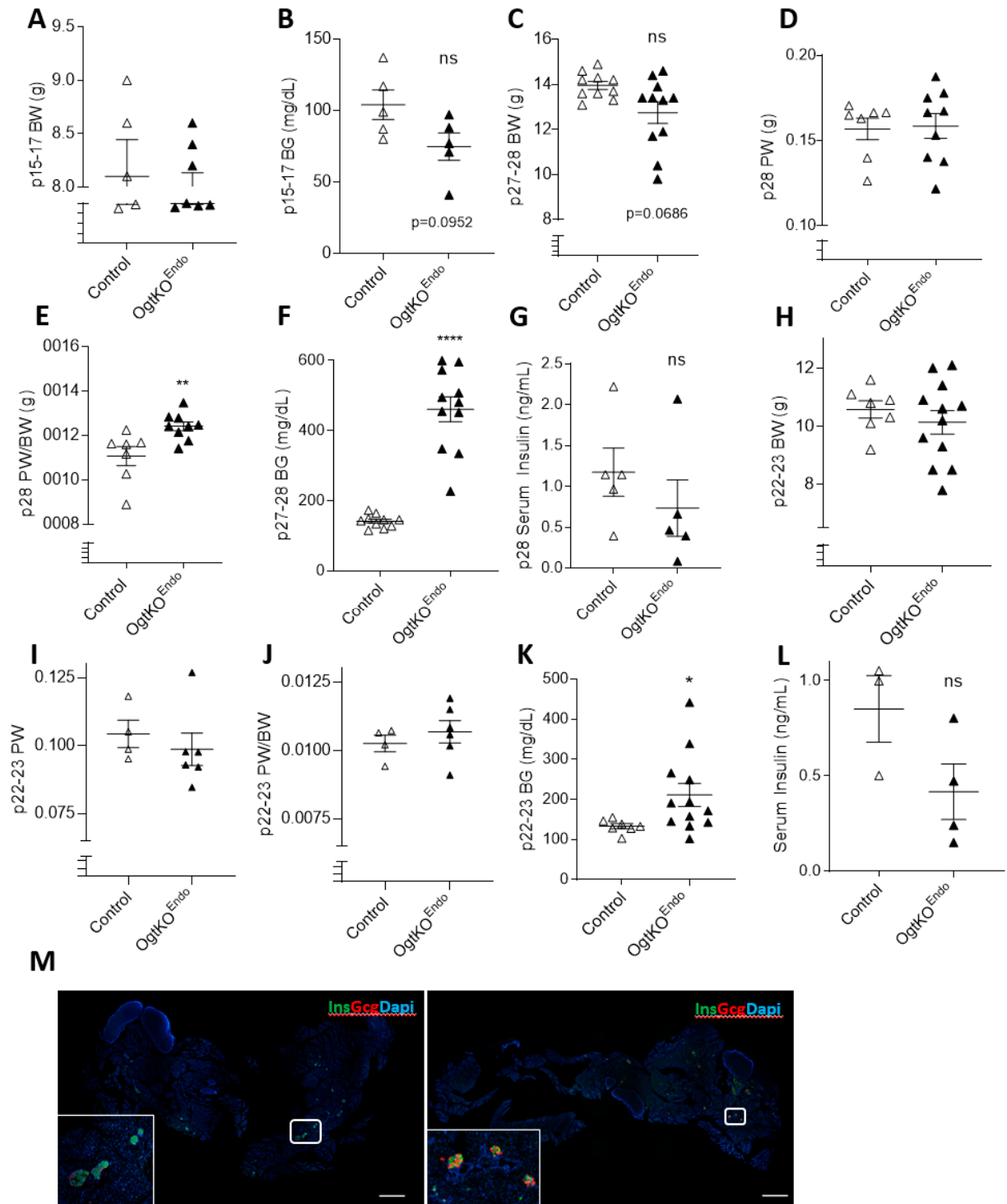
Supplemental Figure S2. Female OgtKO[Endo] develop progressive hyperglycemia over time. Body weight (**A**, $n = 5–7$) and non-fasting blood glucose (**B**, $n = 5$, $p = 0.0952$) at p15–17. Body weight (**C**, $n = 10–11$, $p = 0.0686$), pancreas weight (**D**, $n = 7–9$), pancreas/body weight (**E**, $n = 7–9$, **$p = 0.0052$), non-fasting blood glucose (**F**, $n = 10–11$, ****$p < 0.0001$), and serum insulin (**G**, $n = 5$) at p27-28. Body weight (**H**, $n = 7–12$), pancreas weight (**I**, $n = 4–6$), pancreas/body weight (**J**, n = 4–6), non-fasting blood glucose (**K**, $n = 7–12$, *p = 0.0171), and serum insulin (**L**, $n = 3–4$) and representative images of pancreas morphology (**M**, 4×, scale bar = 1000 µm) at p23. In all graphs, open triangle = Control and closed triangle = OgtKO[Endo].

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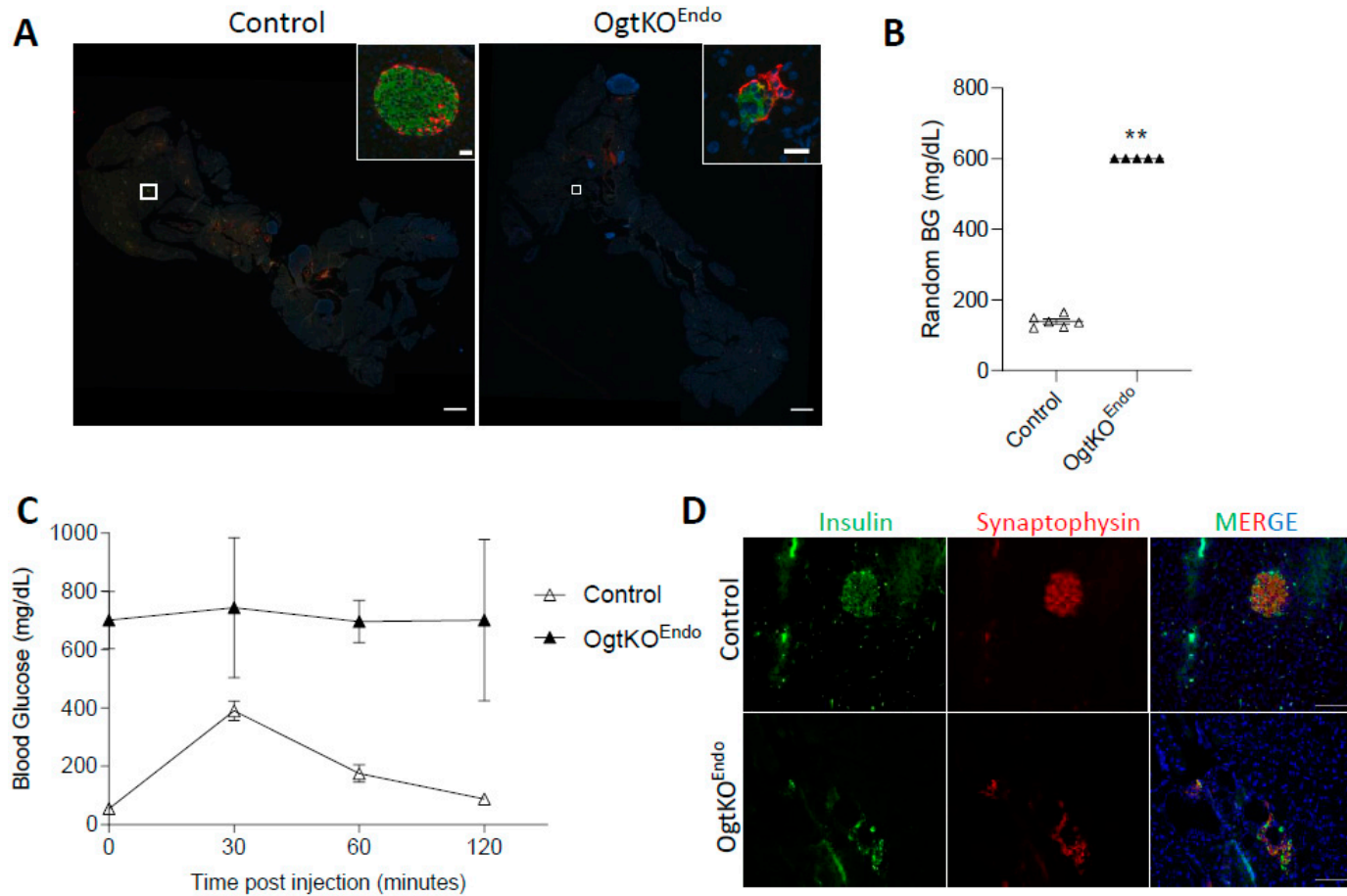
Supplemental Figure S3. Loss of α-cell mass and β-cell mass in OgtKO[Endo] is not compensated by other pancreatic endocrine cells. Representative immunofluorescence images of whole pancreas at p60 (**A**, 10×, scale = 1000 μm). Non-fasting blood glucose in females (**B**, n = 5–6) at p60. Intraperitoneal glucose tolerance test in females (**C**, n = 3–6) at p70. Representative images of islets stained with synaptophysin showing no compensation from other islet cells in the OgtKO[Endo] (**D**, 20×, scale = 50 μm). In all graphs, open triangle = Control and closed triangle = OgtKO[Endo]. **$p \leq 0.01$.