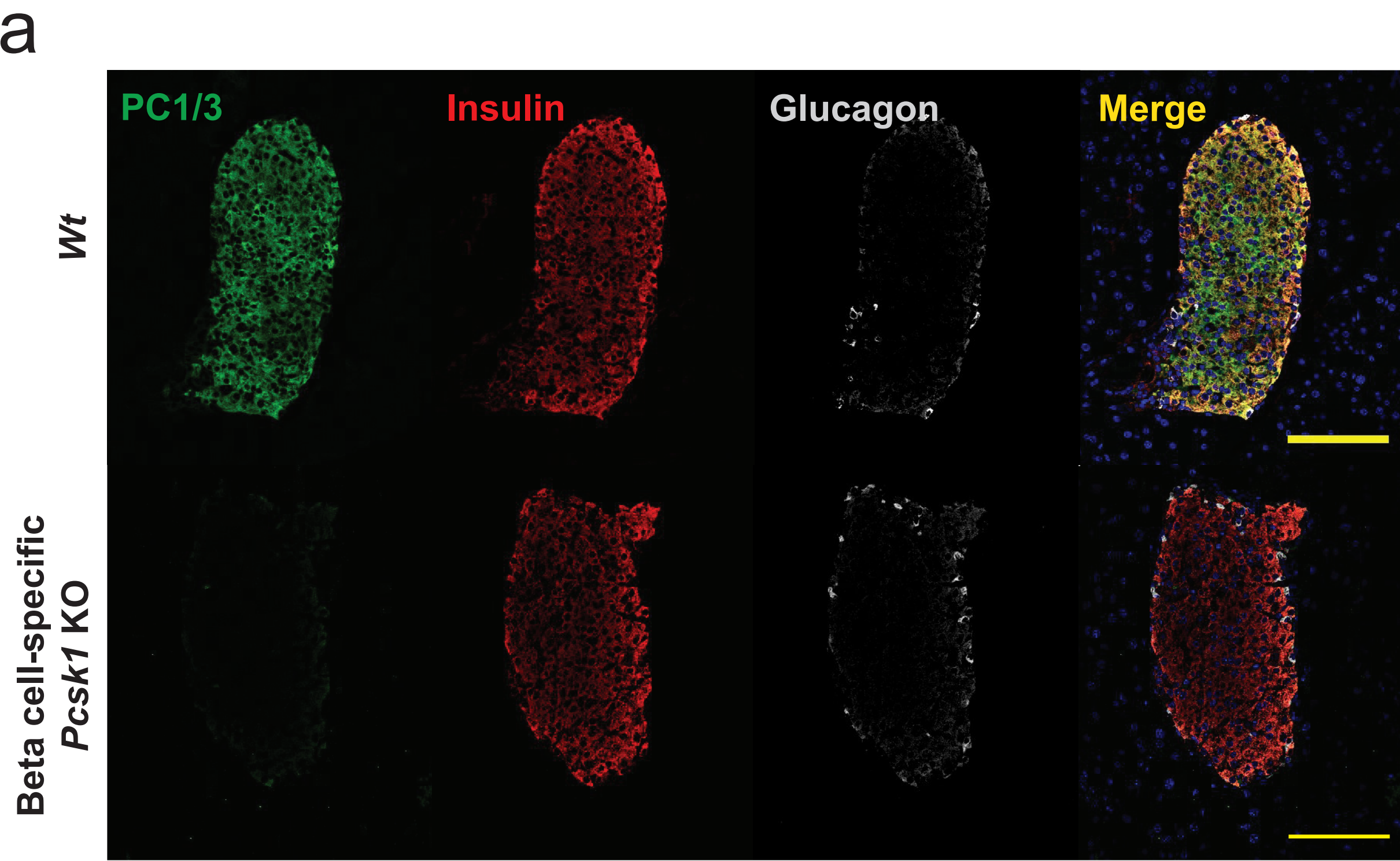


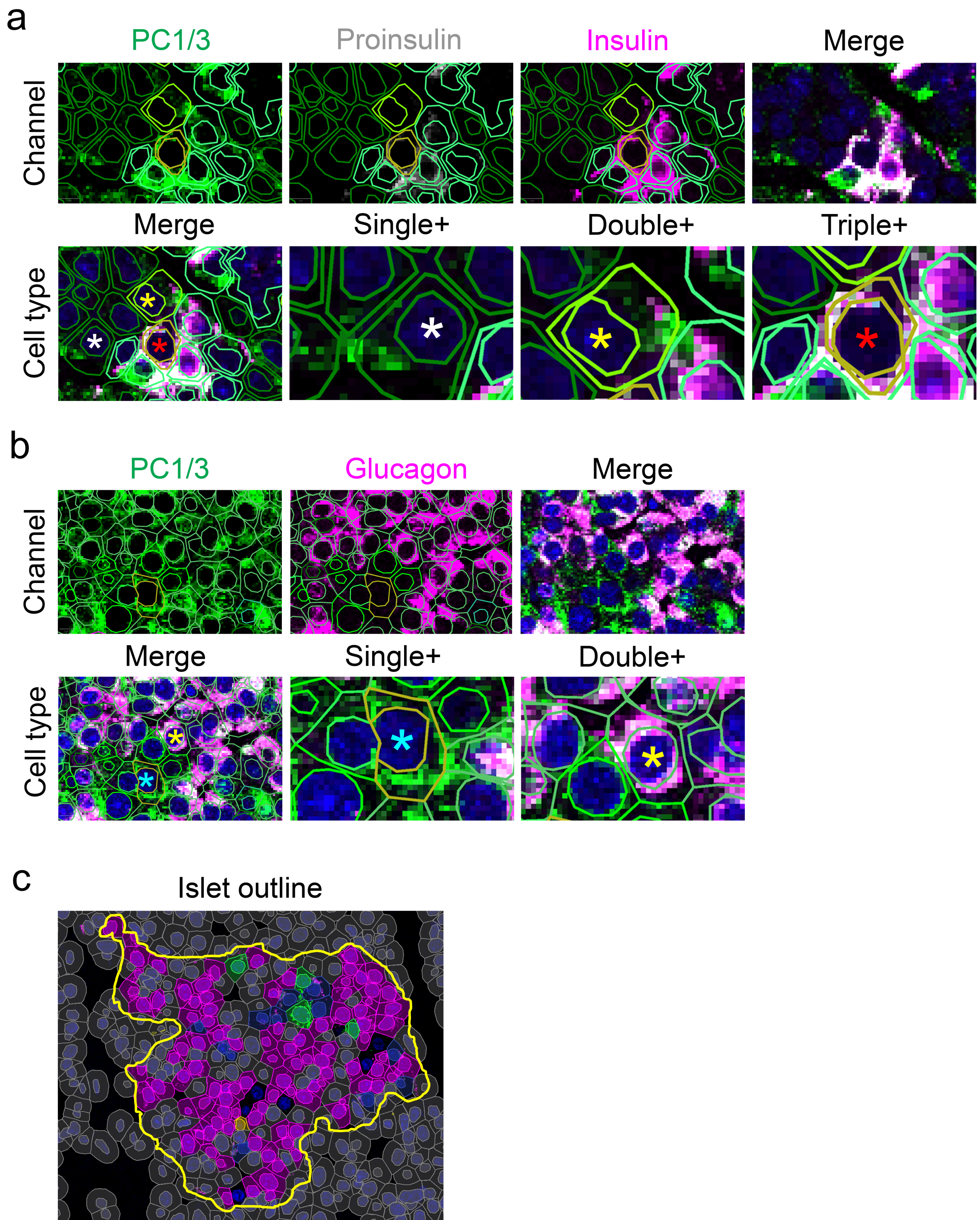


b

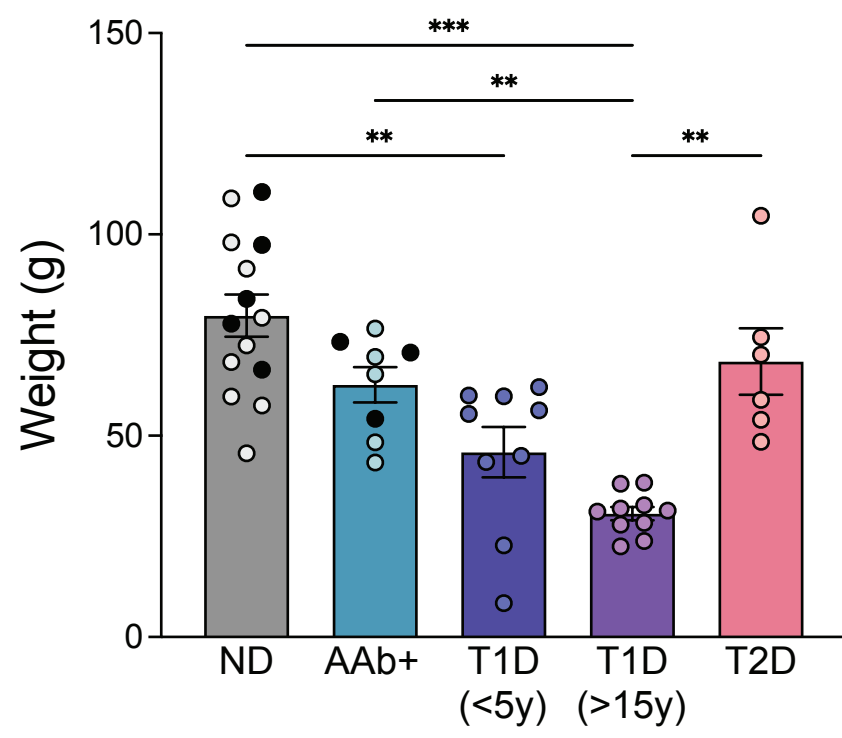
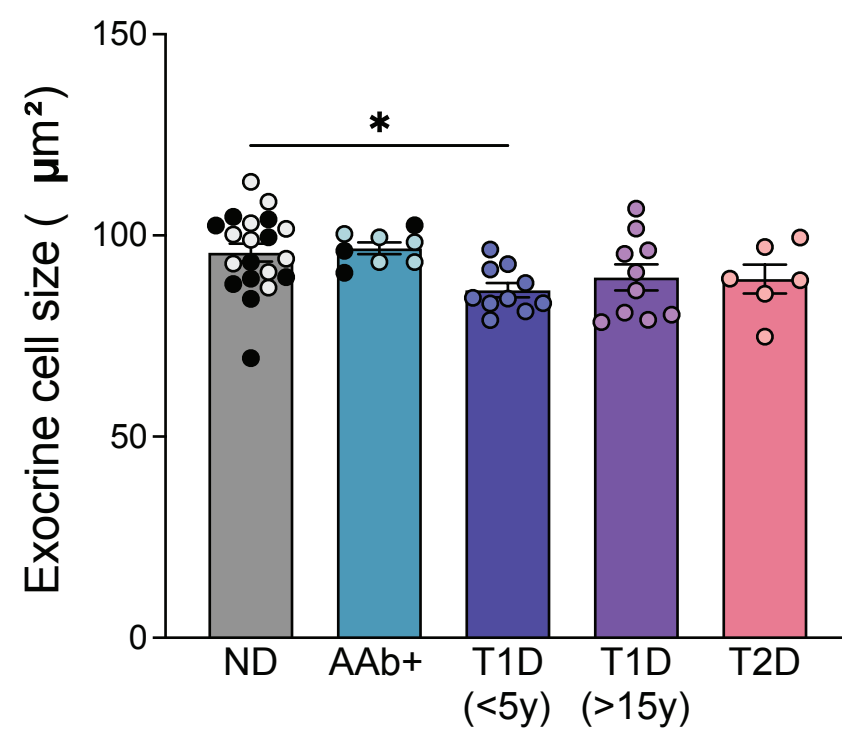
PC1/3 antibody targeting region

NEC1_HUMAN	DVFYNT --- KPYKHRDDRLLQALVDILNEEN-----	753
NEC2_HUMAN	-----	638
PCSK7_HUMAN	-----C-----	785
PCSK9_HUMAN	-----	692
FURIN_HUMAN	TVFLVLQLRSGFSFRGVKVTMDRGLISYKGLPPEAWQEECPDSEEDGRGERTAFIKD	790

ESM. Figure 1 (a) Representative images showing PC1/3, insulin, and glucagon staining in islets from wild-type (*Wt*) and beta cell-specific *Pcsk1* knockout (KO) mice. **(b)** PC1/3 antibody-targeted sequence. NEC1, neuroendocrine convertase PC1, PC1/3; NEC2, neuroendocrine convertase PC2, PC2.



ESM. Figure 2 Representative images showing cell segmentation based on **(a)** PC1/3, proinsulin, and insulin or **(b)** PC1/3 and glucagon staining signals, using QuPath software with StarDist plug-in. Asterisks indicate cells with single-, double-, or triple- markers. **(c)** Representative image showing islet outline generated via advanced cell detection and classification pipelines in QuPath.

a**b**

ESM. Figure 3 (a) Average pancreas weight of non-diabetic donors (ND; filled circle: older adult; empty circle, young adult, n=5 and 9), donors with autoantibodies (AAb+; filled circle: double autoantibody-positive, n=3; empty circle: single autoantibody-positive, n=5), donors with recent-onset T1D (T1D <5y, n=9), long-duration T1D (T1D >15y, n=10) and donors with T2D (n=6). **(b)** Average exocrine cell size in pancreas of non-diabetic donors (ND; filled circle: older adult; empty circle, young adult, n=10 each group), donors with autoantibodies (AAb+; filled circle: double autoantibody-positive, n=3; empty circle: single autoantibody-positive, n=5), donors with recent-onset T1D (T1D <5y, n=10), long-duration T1D (T1D >15y, n=10) and donors with T2D (n=6). Each dot represents the average value from one donor, data are expressed as mean $\pm$ SEM, * p <0.05, ** p <0.01, *** p <0.001.