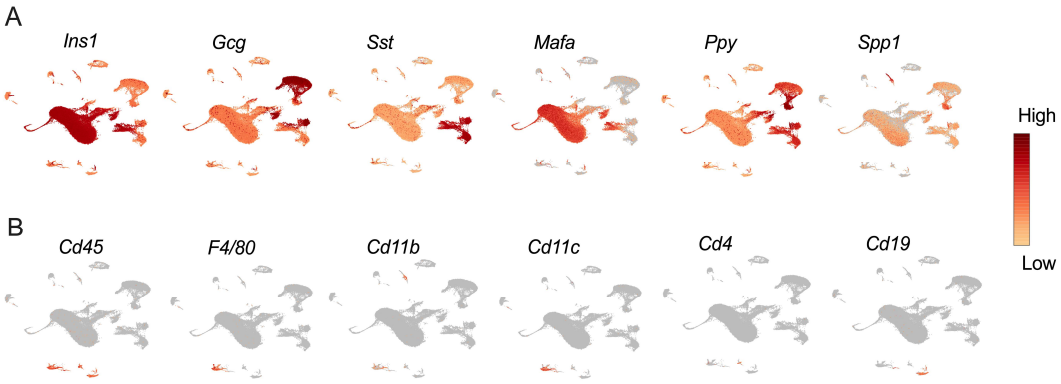
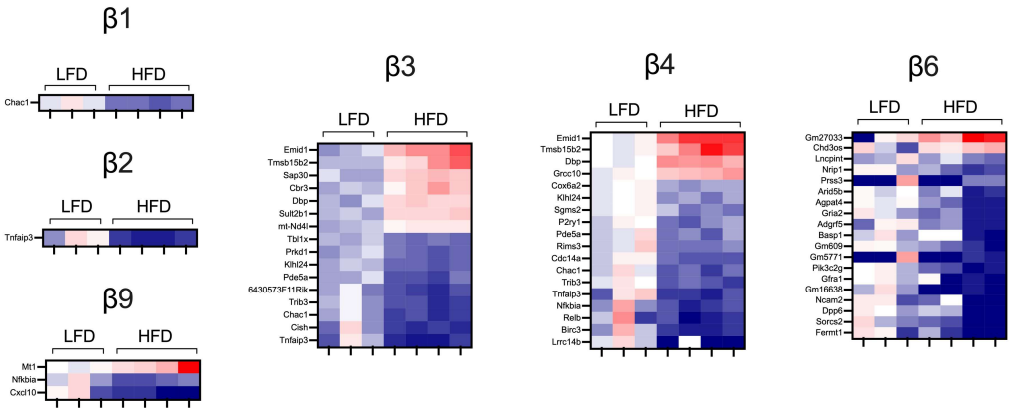
Supplemental Table S1. Percentage of cells per cluster identified by sc-RNAseq.

	LFD1	LFD2	LFD3	HFD1	HFD2	HFD3	HFD4
β cells	69	66	55	67	68	64	58
α cells	12	14	28	16	14	15	16
δ cells	4	7	6	6	6	6	5
Acinar	0	1	2	0	1	4	8
Other	14	11	7	9	10	10	11
Unclassified	2	2	2	3	2	2	2
Total	100	100	100	100	100	100	100



Supplemental Figure S1. Genes used for identification of cell clusters. Single cells were obtained from dissociated islets from male *C57BL/6J* mice fed for one week with either a high fat diet (HFD, 60% kcal from fat) or a control low fat diet (LFD, 10% kcal from fat) and used to perform single-cell RNA sequencing analysis. (**A**) UMAP plots showing spatial expression of identifying genes for the 6 major types of endocrine cells: *Ins1, Gcg, Sst, Mafa, Ppy, Spp1;* (**B**) Expression markers for 5 major populations of immune cells: *Cd45, F4/80, Cd11b, Cd11c, Cd4* and *Cd19*. Color assignments represent levels of expression.



Supplemental Figure S2. Identification of differentially expressed genes of the major β cell clusters. β-cell clusters were identified from dissociated islets from male *C57BL/6J* mice fed for one week with either a high fat diet (HFD, 60% kcal from fat) or a control low fat diet (LFD, 10% kcal from fat). Shown are heatmaps of the major β-cell clusters of genes significantly differentially expressed ($p < 0.05$) in the β-cell clusters; genes are ordered from most positive to most negative fold-change.