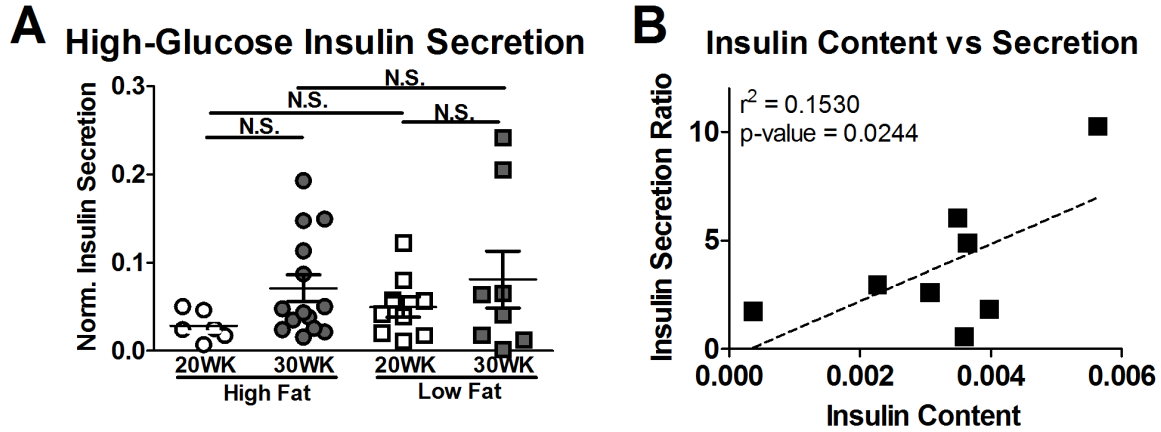


Supplemental Figure 1. Islet area histogram (left) and density plot (right) for each cohort, 20-week high fat (A), 30-week high fat (B), 20-week low fat (C), and 30-week low fat (D). Dashed line shows islet size threshold. N= 2,333-10,380 islets per cohort.



Supplemental Figure 2. Normalized insulin secretion in response to elevated (11 mM) glucose (A). Islet insulin content vs glucose-stimulated insulin secretion for low fat-fed mice (B). A, N =5-14 individuals per cohort. B, N = 8. N.S. – Not significant

Supplemental Table 1. Cohort metrics for islet mass quantification.

Cohort	Individuals	Female /Male Ratio	Slides	Total Islets	Total Islet Area (μm^2)	Avg Islet Area (μm^2)	Islets/Slide	Area/Slide	Total Tissue Area (μm^2)	Islet Area/Tissue Area
20 HF	16	0.5	62	8,320	132,564,412	15,933	134.2	2,138,136	496,461,183	0.27
30 HF	16	0.5	64	10,380	194,565,474	18,744	162.2	3,040,086	512,715,812	0.38
20 LF	12	0.5	48	2,333	19,956,617	8,554	48.6	415,763	176,863,435	0.11
30 LF	11	0.64	40	3,141	28,581,981	9,100	78.5	714,550	198,371,139	0.14