Online Only Supplemental Material

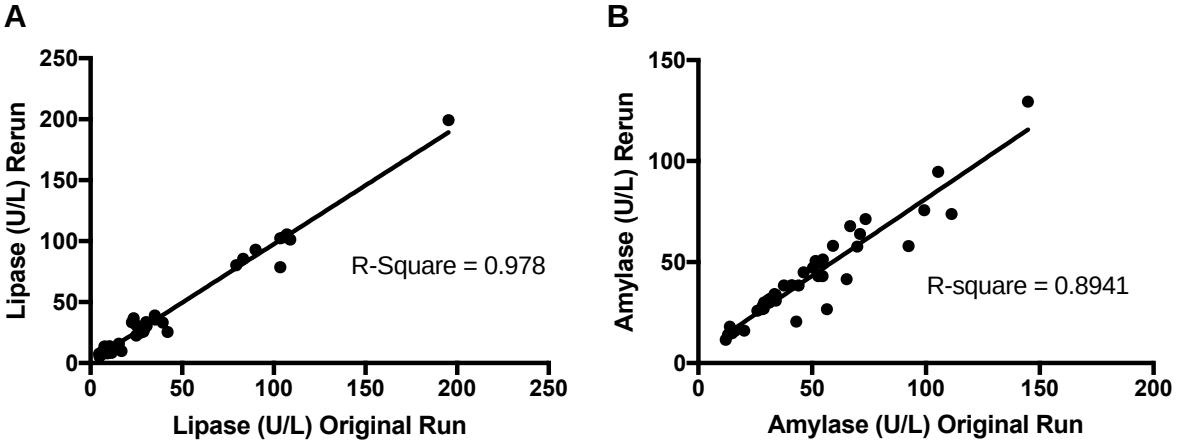

Figure S1. Linear regression analysis of pancreatic exocrine enzyme technical replicates. To assess longitudinal stability of amylase and lipase in frozen serum, 42 Cohort 1 samples were randomly selected to be re-tested for (A) lipase and (B) amylase seven months after the original run.

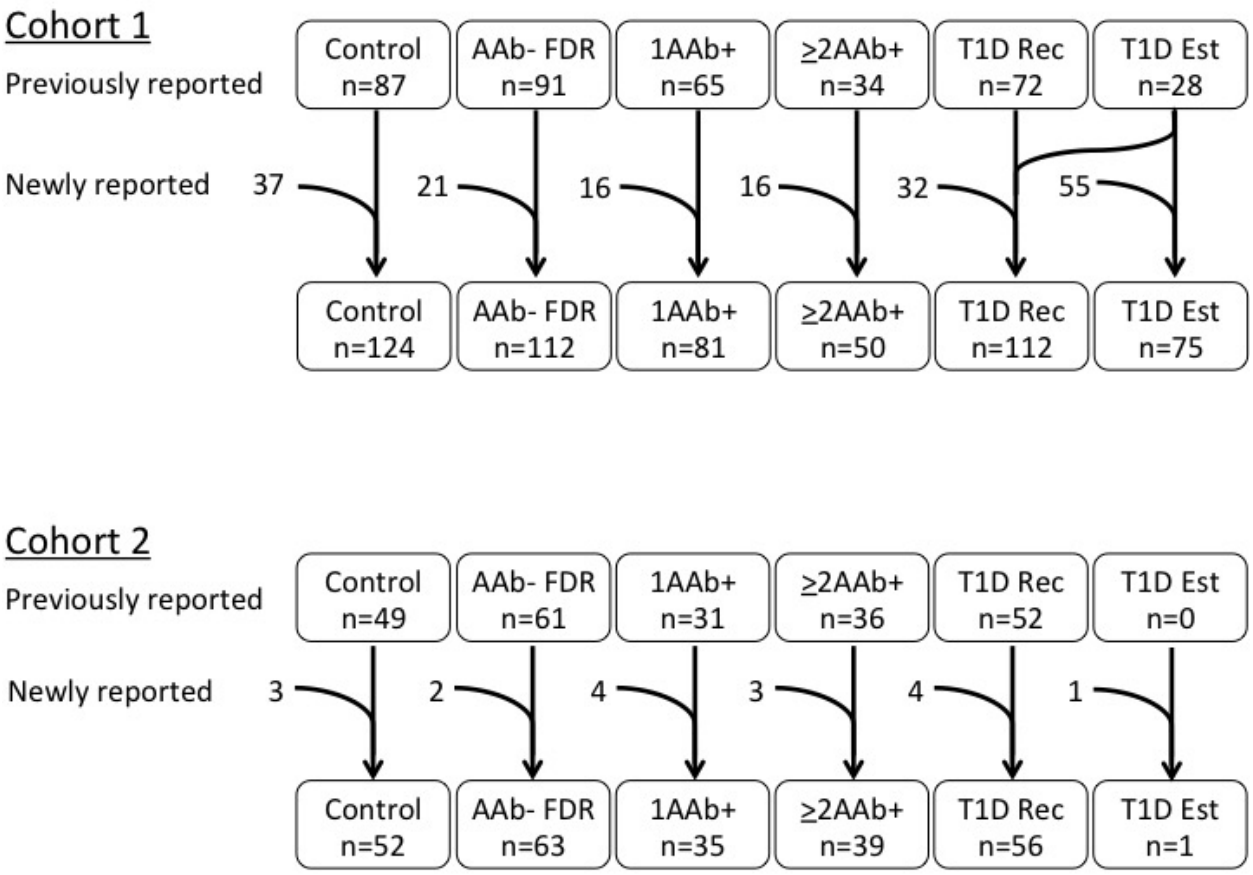

Figure S2. Flow diagram displaying previously and newly reported subjects. For Cohort 1, the current analysis includes serum trypsinogen levels from 377 previously reported (1) and 177 newly reported individuals as indicated on the figure. In the current analysis, the cutoff for recent-onset versus established type 1 diabetes was raised from 3 months to 1 year for consistency with Cohort 2 criteria. This resulted in reclassification of eight previously reported individuals. For Cohort 2, the current analysis includes serum trypsinogen levels and BMI-normalized relative pancreas volume (RPV_{BMI}) from 229 previously reported (2) and 17 newly reported individuals as indicated on the figure. Amylase and lipase data are newly reported for all 800 subjects. Abbreviations: autoantibody negative (AAb-), first degree relatives (FDR), single AAb positive (1AAb+), multiple AAb+ (≥2AAb+), recent onset type 1 diabetes (T1D Rec), established T1D (T1D Est).

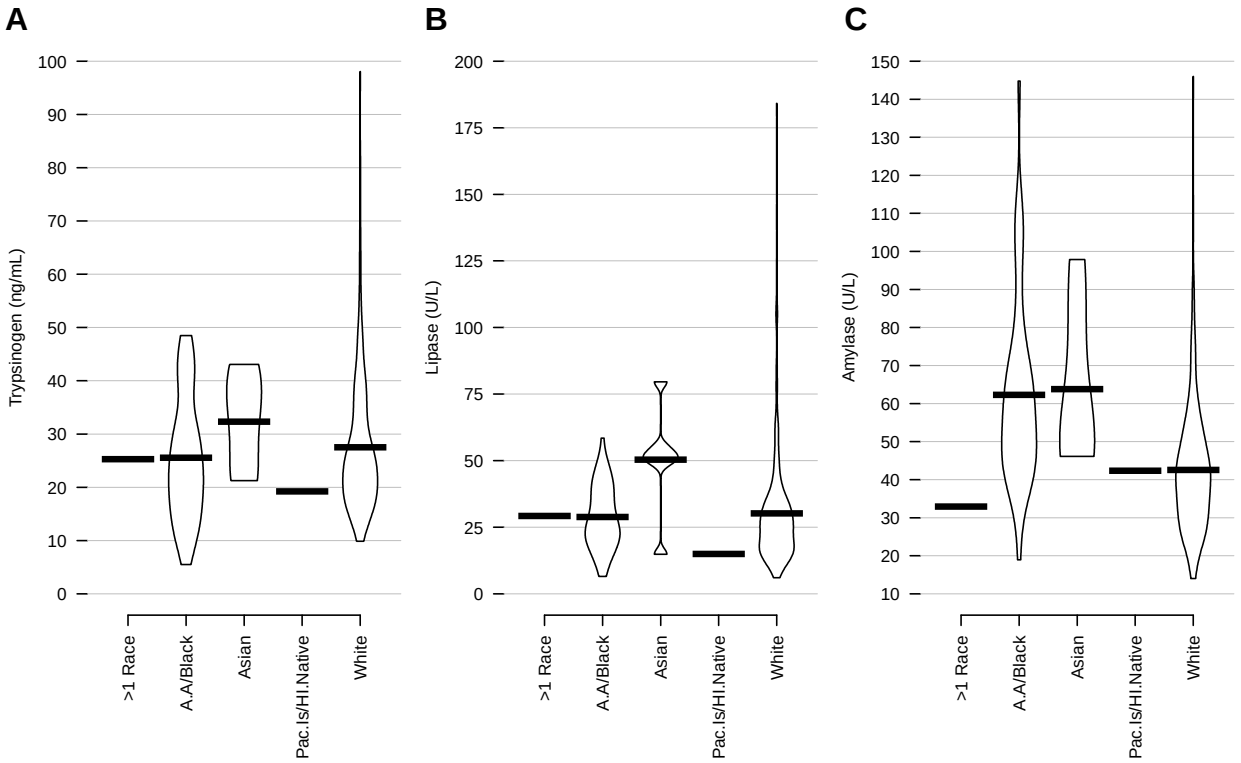

Figure S3. Exocrine pancreatic enzyme levels versus race in islet autoantibody negative (AAb-) subjects. Violin plots show serum levels of (A) trypsinogen, (B) lipase, and (C) amylase for AAb- subjects grouped according to self-reported race. One individual reporting as American Indian/Alaska Native and 10 individuals with unknown race were removed for the purpose of this analysis. Data are shown as violin plots with mean ± standard deviation (SD) and analyzed by one-way ANOVA (trypsinogen $P > 0.05$, lipase $P < 0.05$, and amylase $P < 0.001$).

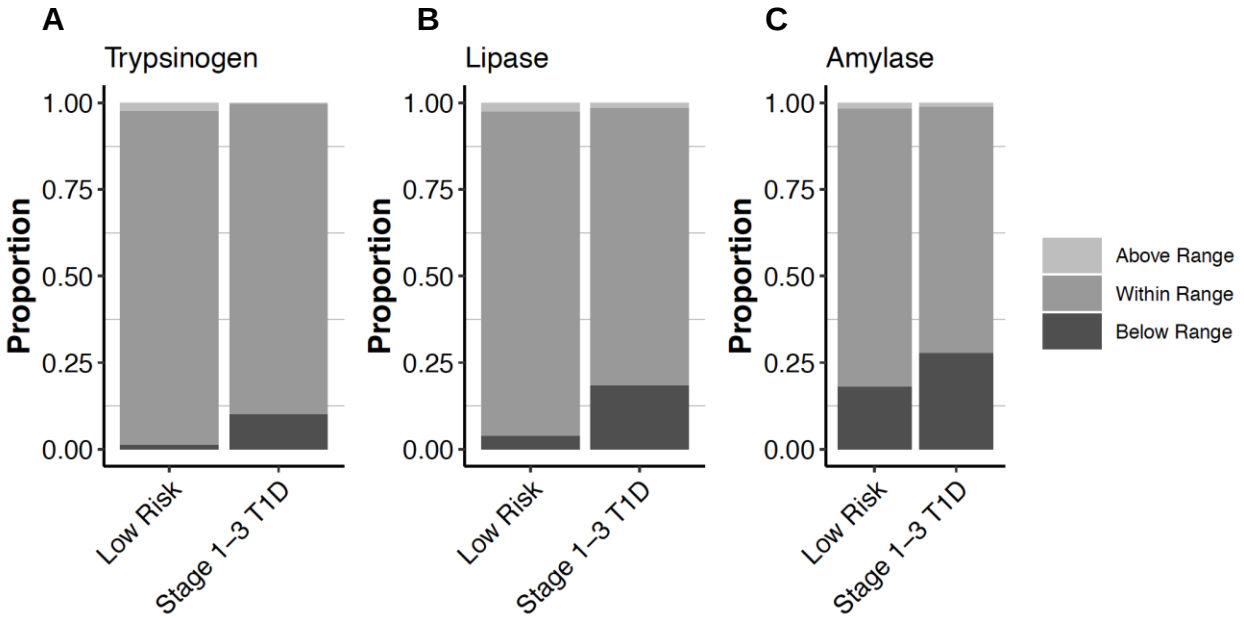

Figure S4. Exocrine pancreas enzyme levels. The proportions of subjects having serum levels of (A) trypsinogen, (B) lipase, or (C) amylase below (dark), within (medium), or above (light) the clinical reference range are shown for subjects classified as having Low Risk for type 1 diabetes (AAb- controls, AAb- FDR, and 1AAb+) versus Stage 1-3 disease (≥2AAb+, recent-onset type 1 diabetes, and established type 1 diabetes). Data were analyzed by chi-square test (trypsinogen $P < 0.001$, lipase $P < 0.001$, and amylase $P < 0.002$).

SUPPLEMENTAL REFERENCES

1. Li X, Campbell-Thompson M, Wasserfall CH, McGrail K, Posgai A, Schultz AR, et al. Serum Trypsinogen Levels in Type 1 Diabetes. *Diabetes Care.* 2017;40(4):577-82.
2. Campbell-Thompson ML, Filipp SL, Grajo JR, Nambam B, Beegle R, Middlebrooks EH, et al. Relative Pancreas Volume Is Reduced in First-Degree Relatives of Patients With Type 1 Diabetes. *Diabetes Care.* 2019;42(2):281-7.