P: Genetics—Type 2 Diabetes| June 20, 2023

1470-P: Novel Associations of Glycometabolic Traits in Ethnically Diverse Africans

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Diabetes 2023;72(Supplement_1):1470-P

https://doi.org/10.2337/db23-1470-P

Prior studies have identified genetic factors that impact an individual's risk of developing type 2 diabetes (T2D). However, African ancestry is underrepresented in genetic studies despite the higher prevalence of T2D in African Americans compared to European or Asian Americans. To better understand risk factors for this health disparity, we used a unique dataset of T2D biomarkers (C-peptide and standing glucose) and ~5 million single nucleotide polymorphism genotypes from an ethnically diverse sampling of sub-Saharan Africans (N~1,250) to identify genetic variants associated with these traits. Because the individuals in our dataset practice traditional subsistence patterns and live in rural settings, there is less environmental heterogeneity than observed in urban settings. Between both traits, we uncovered hundreds of novel marginal associations ($p<10^{-5}$) and three genome-wide significant associations ($p<5\times10^{-8}$), one with C-peptide (rs147703855, in *DAAM1*) and two with glucose (rs74085215, near *KLC1*; rs951516, intergenic). The minor alleles for these three associations are rare outside of Africa (<0.1%) but attain frequencies ~5-10% in at least one African ancestry group. Although none of these associations have been previously reported, the genes near the marginal C-peptide associations (<200kbp) are enriched for variants with previously reported T2D associations (GWAS catalogue), as well as chylomicron, VLDL, and triglyceride associations. The genes near our marginal glucose associations were not found to be enriched for previously reported T2D associations ($p>0.05$), though they were significantly enriched for body size, chylomicron, and triglyceride associations ($p<0.006$). We are following up this preliminary study with an expanded GWAS using a new proteomics dataset in ~500 subjects, and a metabolomics dataset in ~700 subjects. These data will be used to construct polygenic risk scores for biomarkers of T2D that are more effective in people of recent African descent.