Type 2 Diabetes (T2D) and Quantitative Trait Association Analysis of a Finnish Sample with SNPs Previously Reported to be Associated with T2D

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The Finland-United States Investigation of NIDDM Genetics (FUSION) study aims to identify genetic variants that predispose to T2D or are responsible for variability in diabetes-related quantitative traits. We performed a comprehensive literature search to survey previously reported associations between T2D status and single nucleotide polymorphisms (SNPs). We found reports of significant associations with 106 SNPs in 55 genes. We had previously analyzed 13 of these SNPs for association in 795 cases and 426 controls and confirmed association for one SNP in *PPARG*. More recently, we successfully genotyped an additional 52 SNPs on 795 cases and 650 controls (426 initial plus 224 new samples) and replicated association in 9 of 52 SNPs. The SNP minimal p-values for disease association as assessed by 4 genetic models, ranged from 0.0005 to 0.012. We next examined whether the SNPs previously reported to be associated with T2D were associated with diabetes-related quantitative traits (QTs). QTs were derived from clinical measures, oral glucose tolerance tests (OGTTs), and frequently sampled intravenous glucose tolerance tests (FSIGTs) with minimal model analysis. We performed permutation tests to assess overall significance to account for multiple testing. For 8 SNPs representing 7 genes, we found significant phenotype associations in the normoglycemic individuals >65 years of age ($P < 0.05$), whereas we would expect < 3 by chance. Interestingly, 1 SNP from the *TNF-alpha* gene exhibited both disease and QT associations. These data suggest that these genetic variants, or others in close LD, may play a role in pathogenesis of T2D.