Quantitative candidate gene association studies of metabolic traits in Han Chinese type 2 diabetes patients

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ABSTRACT. Recent genome-wide association studies have identified many loci associated with type 2 diabetes mellitus (T2DM), hyperuricemia, and obesity in various ethnic populations. However, quantitative traits have been less well investigated in Han Chinese T2DM populations. We investigated the association between candidate gene single nucleotide polymorphisms (SNPs) and metabolic syndrome-related quantitative traits in Han Chinese T2DM subjects. Unrelated Han Chinese T2DM patients (1975) were recruited. Eighty-six SNPs were genotyped and tested for association with quantitative traits including lipid profiles, blood pressure, body mass index (BMI), serum uric acid (SUA), glycated hemoglobin (HbA1c), plasma glucose [fasting plasma glucose (FPG)], plasma glucose 120 min post-OGTT (P2PG; OGTT = oral glucose tolerance test), and insulin resistance-related traits. We found that CAMTA1, ABI2, VHL, KAT2B, PKHD1, ESR1,
TOX, SLC30A8, SFI1, and MYH9 polymorphisms were associated with HbA1c, FPG, and/or P2PG; GCK, HHEX, TCF7L2, KCNQ1, and TBX5 polymorphisms were associated with insulin resistance-related traits; ABCG2, SLC2A9, and PKHD1 polymorphisms were associated with SUA; CAMTA1, VHL, KAT2B, PON1, NUB1, SLITRK5, SMAD3, FTO, FANCA, and PCSK2 polymorphisms were associated with blood lipid traits; CAMTA1, SPAG16, TOX, KCNQ1, ACACB, and MYH9 polymorphisms were associated with blood pressure; and UBE2E3, SPAG16, SLC2A9, CDKAL1, CDKN2A/B, TCF7L2, SMAD3, and PNPLA3 polymorphisms were associated with BMI (all P values <0.05). Some of the candidate genes were associated with metabolic and anthropometric traits in T2DM in Han Chinese. Although none of these associations reached genome-wide significance (P < 5 x 10^-8), genes and loci identified in this study are worthy of further replication and investigation.

**Key words:** Type 2 diabetes mellitus; Association study; Candidate genes; Quantitative traits; Insulin resistance