Meta-analysis of association of common variants in the KCNJ11-ABCC8 region with type 2 diabetes

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ABSTRACT. KCNJ11 (potassium inwardly rectifying channel, subfamily J, member 11) and ABCC8 (ATP-binding cassette, subfamily C (CFTR/MRP), member 8) have been studied for association with type 2 diabetes in various ethnic populations with contradictory results. We performed a comprehensive meta-analysis for KCNJ11 rs5219, rs5210, rs5215, and ABCC8 rs757110 to evaluate the effect of these regions on genetic susceptibility for type 2 diabetes. Forty-one case-control association studies of KCNJ11 and ABCC8 polymorphisms with type 2 diabetes, including 61,879 subjects, were identified and used in our meta-analysis. Combined odds ratios (OR) of associations of this disease with the rs5219 T, rs5210 G, rs5215 G, and rs757110 G alleles were 1.15 [95% confidence interval (95%CI) = 1.10-1.21, P < 0.0001], 1.16 (95%CI = 1.08-1.24, P = 0.023), 1.08 (95%CI = 1.02-1.13, P = 0.006), and 1.12 (95%CI = 1.07-1.18, P < 0.0001), respectively. The effect of allele T of rs5219 was similar (OR = 1.16) in Europeans and Japanese. However, rs5219 was not associated with type 2 diabetes in the Chinese Han population. Our meta-analysis demonstrated that KCNJ11 and ABCC8 polymorphisms are associated with risk for type 2 diabetes in the global population. Comparative genomics and bioinformatics
analyses revealed that rs5210 is located within a conserved 3'-UTR, and that allele A may abolish the binding site of hsa-miR-1910 that the risk allele G possesses.

**Key words:** *ABCC8; KCNJ11; Type 2 diabetes; miRNA; Meta-analysis*