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Multivariate Analysis of identifying novel genetic variants for Metabolic Syndrome in Korean Cohorts

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Metabolic syndrome (MetS) is a complex disease related to insulin resistance, obesity, triglyceride, HDL-cholesterol, blood pressure, and fasting glucose. Most genome-wide association studies (GWAS) have traditionally focused on a single phenotype to identify genetic factors linked to complex diseases. However, despite the considerable successes achieved through GWAS, only a small number of disease-causing genetic factors have been identified by very stringent genome-wide significance criterion. Moreover, these identified genetic factors explain only a fraction of the heritability of MetS. To address this limitation, we conducted a multiple-phenotype genome-wide association analysis using Multiple Phenotype Association Tests (MPAT). For this study, we applied the MPAT approaches to the Korea Biobank Array (K-Chip) datasets obtained from population-based cohorts in the Korean Genome and Epidemiology Study (KoGES), including a discovery cohort (the Ansan and Ansung study, with 1490 cases and 3856 controls) and two replication cohorts (the Cardiovascular Disease Association Study (CAVAS) with 3620 cases and 4461 controls, and the Health Examinee (HEXA) study with 15257 cases and 41807 controls). After adjusting for age, sex, and area (only in the Ansan and Ansung study), we found that rs662799, located in the *APOA5* gene, was significantly associated with MetS using logistic regression analysis. On the other hand, we identified a total of 23 single nucleotide polymorphisms (SNPs) with genome-wide significance levels (p-values $< 1.566 \times 10^{-7}$) using the MPAT approaches. Among these 23 SNPs, eighteen were previously reported to be associated with any components of MetS. In conclusion, our findings offer valuable insights into understanding the underlying mechanisms of MetS by elucidating its genetic etiology.