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Transcriptome-Wide Association Studies of 81 traits in 79,294 individuals from Korean Populations

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Numerous genetic loci have been firmly linked to complex traits by genome-wide association studies (GWAS). Although, GWAS loci are often difficult to interpret because linkage disequilibrium (LD) often masks the causal variants driving the association, and GWAS data alone rarely revealed the causal genes mediating variant effects on the trait and had multiple testing burden. To overcome these limitations, transcriptome-wide association studies (TWAS) have emerged, using predicted gene expression to identify genomic risk regions associated with complex traits and diseases. However, the reference panels for the TWAS study were composed mostly of Europeans. This predominant focus on Europeans in large-scale genetic studies overlooked global genetic diversity, potentially compromising the accuracy of genetic inference in non-European populations. Here, we generated a Korean-specific whole blood reference panel for transcriptome imputation and applied it for TWAS analyses for 81 traits. We demonstrated the improved predictive performance of the reference panel and identified 470 significant gene-trait associations (Bonferroni-corrected p-value < 0.05). We also identified 194 novel gene-trait associations. This study demonstrated that the ethnic-specific approach is essential to more fully understand the genetic architecture of complex diseases, highlighting the value of including diverse populations in genetic research.