Publication

1000 Genomes-based meta-analysis identifies 10 novel loci for kidney function

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HapMap imputed genome-wide association studies (GWAS) have revealed >50 loci at which common variants with minor allele frequency >5% are associated with kidney function. GWAS using more complete reference sets for imputation, such as those from The 1000 Genomes project, promise to identify novel loci that have been missed by previous efforts. To investigate the value of such a more complete variant catalog, we conducted a GWAS meta-analysis of kidney function based on the estimated glomerular filtration rate (eGFR) in 110,517 European ancestry participants using 1000 Genomes imputed data. We identified 10 novel loci with p-value < 5 Œ 10(-8) previously missed by HapMap-based GWAS. Six of these loci (HOXD8, ARL15, PIK3R1, EYA4, ASTN2, and EPB41L3) are tagged by common SNPs unique to the 1000 Genomes reference panel. Using pathway analysis, we identified 39 significant (FDR < 0.05) genes and 127 significantly (FDR < 0.05) enriched gene sets, which were missed by our previous analyses. Among those, the 10 identified novel genes are part of pathways of kidney development, carbohydrate metabolism, cardiac septum development and glucose metabolism. These

results highlight the utility of re-imputing from denser reference panels, until whole-genome sequencing becomes feasible in large samples.
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