


 TRANSLATIONAL GENOMICS

# A network of the human metabolome

Genome-wide association studies (GWASs) have yielded several novel associations between genetic variants and human disease phenotypes. Now, Shin *et al.* have used a similar approach that correlates genetic variants with metabolites isolated from human blood to produce a catalogue of genetic influences on the blood metabolome.

The investigators initially used chromatography and mass spectrometry to characterize and quantify the metabolites in plasma or serum samples from 7,824 healthy twin and singleton adults who were enrolled in 2 European studies. They identified

529 metabolites from 63 biochemical pathways that fall into broad metabolic groups such as carbohydrates, lipids and amino acids, and categorized them by heritability. The researchers then carried out genome-wide discovery analysis by genotyping the same samples and correlated these data with the metabolite data. Through this approach, they identified 299 associations between single-nucleotide polymorphisms (SNPs) and metabolites at 145 loci. They then produced a searchable network to show how these metabolites relate to each other and how they connect to the various metabolic genetic loci identified.

Using data from the National Human Genome Research Institute GWAS catalogue, the authors further annotated their network by correlating the

metabolite-associated SNPs they found with 55 SNPs that are associated with a complex trait or disease. They then searched for correlations between the metabolic genes identified and genes that are established or promising drug targets, which had been identified by the US Food and Drug Administration or the European Medicines Agency. This allowed them to show that “genes of pharmacological relevance (transporters, drug metabolizing enzymes and particularly drug targets) are significantly associated with metabolomic loci”, according to Nicole Soranzo (Wellcome Trust Sanger Institute), one of the senior authors of the study.

This network provides a comprehensive map of blood metabolite–gene interactions and is a useful tool for uncovering the genetic basis of differences in human metabolism that affect a multitude of human diseases.

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**ORIGINAL RESEARCH PAPER** Shin, S.Y., *et al.*  
An atlas of genetic influences on human blood metabolites. *Nature Genet.* <http://dx.doi.org/10.1038/ng.2982> (2014)