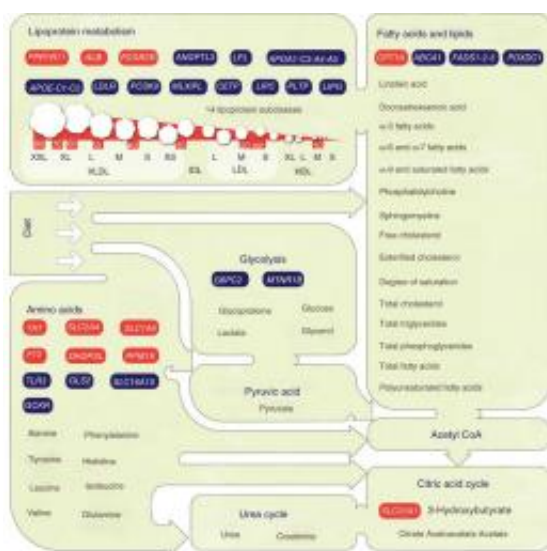


Genetic regulation of metabolomic biomarkers -- paths to cardiovascular diseases and type 2 diabetes

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Overall summary of basic metabolism, key constituents of the serum metabolome and associated genetic regions. [doi:10.1038/ng.10730]

In a study to the genetic variance of human metabolism, researchers have identified thirty one regions of the genome that were associated with levels of circulating metabolites, i.e., small molecules that take part in various chemical reactions of human body. Many of the studied metabolites are biomarkers for cardiovascular disease or related disorders, thus the loci uncovered may provide valuable insight into the biological processes leading to common diseases.

Laboratory tests used in the clinic typically monitor one or few circulating metabolites. The researchers at the Institute for Molecular Medicine Finland (FIMM) used a high throughput method called [nuclear magnetic resonance](#) (NMR) that can measure more than hundred different metabolites in one assay. This provides a much more in-depth picture of circulating metabolic compounds.

"Using this extensive analysis in thousands of people, we could identify a large number of [genetic loci](#) regulating the level of compounds circulating in the blood stream", says Dr. Samuli Ripatti, the leader of the study.

The team assayed 117 detailed metabolic markers, including lipoprotein subclasses, [amino acids](#) and lipids, and conducted the largest genome-wide association analysis of this type, in terms of study sample size of 8330 individuals from six Finnish population-based cohorts and 7.7 million genomic markers studied. They revealed, in total, 31 genetic regions associated with the blood levels of the metabolites.

Eleven of the loci had not been previously shown to be associated with any metabolic measures.

Among the findings were two new loci affecting serum cholesterol subclass measures, well-established risk markers for cardiovascular disease, and five new loci affecting levels of amino acids recently discovered to be potential biomarkers for type 2 diabetes. The discovered variants have significant effects on the metabolite levels, the effect sizes being in general considerably larger than the known common variants for complex disease have.

Also, using Finnish twin pair samples, the researchers indicated that the metabolite levels show a high degree of heritability. "This result suggests that the studied metabolites are describing better the underlying biology

than the routinely used laboratory tests. Therefore, the study provides further support for the use of detailed data on multitude of metabolites in genetic studies to provide novel biological insights and to help in elucidating the processes leading to [common diseases](#)", Dr. Ripatti says.

Provided by University of Helsinki

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