A comprehensive atlas of genetic regulation of lipid metabolism published

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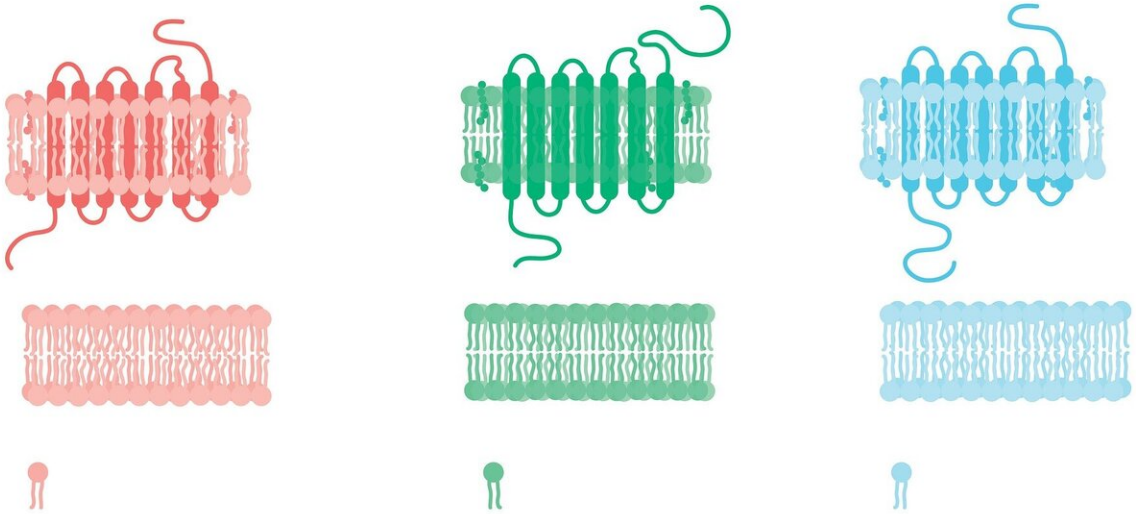

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An international research team has identified several novel genetic variants associated with plasma levels of lipid species and cardiovascular disease risk in humans. The study demonstrates that genetic studies focusing on circulating molecular lipid levels over traditional lipid measures can help improve cardiovascular risk prediction and treatment.

The results of the study led by researchers from the University of

Helsinki have recently been published in the scientific journal *Nature Communications* and are available at mqtl.fimm.fi.

Cardiovascular diseases are the leading cause of mortality and morbidity worldwide, necessitating the need for better preventive and predictive strategies. Plasma lipids are well-established heritable risk factors for cardiovascular diseases and traditional lipids such as total cholesterol and triglycerides are routinely monitored to assess the risk for cardiovascular diseases.

However, these standard lipid measures do not capture the hundreds of diverse molecular components called lipid species that human plasma comprises. Many of these lipid species are risk factors for cardiovascular disease.

In this study, the researchers utilized both genomics and lipidomics (large-scale lipid analysis) approaches. This is the first large-scale study of this type, with access to genome-wide data, lipidomics data with 141 lipid species in almost 2200 Finnish study participants and phenome-wide data for over 500,000 individuals. The genome-wide analyses identified 35 genetic loci that were associated with the level of at least one of the studied lipid species.

Furthermore, the results demonstrate that, similar to the more traditional cholesterol measures, many of the studied lipid species are also heritable. Despite the expected influence of dietary intake on the circulatory lipids, genetic factors were shown to explain 10 to 54% of the variability.

Next, the researchers wanted to know how the 35 identified genetic variants relate to disease outcomes. For this, the team utilized the large UK Biobank and FinnGen cohorts and scanned the association between the identified variants and 25 phenotypes related to cardiovascular diseases derived from health registry data.

Importantly, ten of the 35 variants influencing lipid metabolism also associated with the risk of developing some cardiovascular disease.

The study also provided clues to the underlying mechanisms of effects of well-known lipid loci on lipid metabolism and cardiovascular disease risk.

"Our results show that lipidomics provides higher statistical power and thus better chances to identify lipid-modulating genetic variants with much smaller sample size than traditional lipid measures," said Rubina Tabassum, the lead author of the study from the Institute for Molecular Medicine Finland FIMM at the University of Helsinki.

In addition to enhancing the current understanding of the genetic determinants of circulating lipids, the study highlights the potential of lipidomics in genetic studies focusing on lipid levels and cardiovascular diseases over traditional lipid measures.

"Our study demonstrates that lipidomics enables much deeper insights into the genetic regulation of lipid metabolism. We hope that the openly available browser will in part help future biomarker and drug target discovery and build our understanding of the pathways connecting genetic variation to cardiovascular and other lipid-related diseases," said Professor Samuli Ripatti from the University of Helsinki, who led the study.

More information: Genetic architecture of human plasma lipidome and its link to cardiovascular disease, *Nature Communications* (2019). DOI: 10.1038/s41467-019-11954-8

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