

Genetic analysis helps dissect molecular basis of cardiovascular disease

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Using highly precise measurements of plasma lipoprotein concentrations determined by nuclear magnetic resonance spectroscopy (NMR), researchers led by Daniel Chasman at Brigham and Women's Hospital and Harvard Medical School in Boston, MA, the Framingham Heart Study in Framingham, and the PROCARDIS consortium in Stockholm, Sweden and Oxford, England performed genetic association analysis across the whole genome among 17,296 women of European ancestry from the Women's Genome Health Study.

This large scale analysis of the effects of common genetic variation on plasma lipoprotein profile, a critical component of cardiovascular risk, identified 43 genetic loci contributing to lipoprotein metabolism, including 10 loci not previously recognized in other whole genome analyses. The findings are published on November 20 in the open-access journal *PLoS Genetics*.

The findings were validated among additional populations of both men and women. The research also quantifies the contribution of common genetic variation to the concentration of plasma lipoproteins according to class, that is low-density lipoprotein (LDL), high-density lipoprotein (HDL), or very [low density lipoprotein](#) (VLDL), as well as size and cholesterol or triglyceride content.

The balance of LDL, HDL, and VLDL particle concentration is firmly established as a measure of cardiovascular risk. These major classes of lipoprotein particles are composed of sub-species that can be categorized

according to size. While the overall concentration of each of the major classes can be estimated by the clinical measures of LDL-cholesterol, HDL-cholesterol, and triglycerides, the determinations of the concentration of the sub-species by NMR methodology in the current study provide a more precise picture of lipoprotein profile. Clinical research is engaged in determining the contribution of each of the sub-species to cardiovascular risk.

"This current genetic analysis complements clinical analysis of [cardiovascular risk](#) by evaluating the genetic contribution to the concentration of each lipoprotein sub-species and helps to delineate genes and metabolic pathways that might be targeted for interventional strategies," noted Dr.

Chasman. He continued "the research can be placed in the larger context of studies that are leveraging knowledge of the human genome to dissect the molecular basis of common diseases, particularly cardiovascular disease, through large scale, genome-wide [genetic analysis](#)."

More information: Chasman DI, Paré G, Mora S, Hopewell JC, Peloso G, et al. (2009) Forty-Three Loci Associated with Plasma Lipoprotein Size, Concentration, and Cholesterol Content in Genome-Wide Analysis. PLoS Genet 5(11): e1000730. [doi:10.1371/journal.pgen.1000730](https://doi.org/10.1371/journal.pgen.1000730)

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