*Press release Second Late Breaking News Session: Lipidomics*

**87th Annual Congress of the European Atherosclerosis Society (EAS)**

**May 26-29th 2019, Maastricht, The Netherlands**

***First large-scale study of the genetics of human plasma lipid species***

*Maastricht, 28th May, 2019* **–** Understanding the genetics of lipid species offers information beyond that provided by routine lipid screening, and can help improve risk prediction and treatment. In the first large-scale study, novel lipid-associated genetic variants were identified, some of which were linked with risk for cardiovascular disease, such as heart attacks and strokes.

Human plasma comprises hundreds of lipid species which differ in chemical structure and function. Many of these are known risk factors for human diseases. Advances in mass spectrometry-driven lipid analysis – lipidomics – has made it possible to study the patient lipidome to a greater extent than is possible with conventional analytical methods. Currently, however, understanding the genetic regulation of molecular lipid species is lacking. Unraveling this information could help in the personalized management of atherosclerosis and heart disease.

In light of this, this collaborative project involving centres in Finland, Germany and the USA integrated information from the lipidome, genome and phenome to answer key questions relating to the heritability of lipid species, including: Which genetic variants influence plasma levels of lipid species? How do these variants relate to disease outcomes and what is the underlying mechanisms?

To gain insights into these questions, the investigators initially performed a genome-wide association study (GWAS) of 141 lipid species in 2,181 individuals, followed by phenome-wide scans (PheWAS) of 37 lipid-related outcomes, including cardiovascular, gastrointestinal and neurological disease, up to 511,700 individuals. The study had a number of novel findings.

* Lipid species are heritable, ranging from 10 to 54 per cent, with the highest heritability in lipids containing polyunsaturated fatty acids (PUFAs). These lipid species with PUFAs also had greater genetic sharing with each other. These findings are important given renewed interest in the role of PUFAs in cardiovascular disease.1
* The GWAS analyses identified 35 gene variants that were associated with lipid species. Using clinical outcome data from the FinnGen and UK Biobank cohorts, the investigators showed that 10 of these variants (at the *APOA5, ABCG5/8, BLK, LPL, FADS2, COL5A1, GALNT16, GLTPD2, MBOAT7* and *SPTLC3* genes) were associated with cardiovascular disease. In addition, gene variants at the *BLK, GALNT16* and *LPL* genes were associated with type 2 diabetes. This information could help drive the development of new treatment targets.
* The study also provided clues to the underlying mechanisms of well-known lipid loci on lipid metabolism and cardiovascular disease risk. Notably, the rs11570891 variant of the gene encoding lipoprotein lipase (LpL) is known to be associated with reduced risk of cardiovascular disease and type 2 diabetes. New information from this study suggests that this association might be mediated by increased activity of LpL, and in turn a decrease in medium length triglycerides.

Lead author, Dr Rubina Tabassum (Institute for Molecular Medicine Finland, University of Helsinki, Finland) commented: ‘This study has identified new genomic loci associated with lipid species and disease risks in humans. In addition to enhancing the current understanding of genetic determinants of circulating lipids, our study also highlights the potential of lipidomics in gene mapping for lipids and cardiovascular disease over the traditional lipid measures. These insights into the genetic regulation of lipid metabolism and its link to human diseases might help guide future biomarker and drug target discovery and disease prevention strategies.’

**LATE BREAKING NEWS: Experimental Atherosclerosis and Genetics**

**Monday 28th May, 15:30-17:00, Anitschkow Hall**

Tabassum R, Rämö JT, Ripatti P, Koskela JT, Kurki M, Karjalainen J, Palta P, Hassan S, Nunez-Fontarnau J, Kiiskinen TTJ, Söderlund S, Matikainen N, Gerl MJ, Surma MA, Klose C, Stitziel NO, Laivuori H, Havulinna AS, Service SK, Salomaa V, Pirinen M, FinnGen Project T, Jauhiainen M, Daly MJ, Freimer N, Palotie A, Taskinen MR, Simons K, Ripatti S. Genetics of human plasma lipidome and its link to diseases susceptibility. Abstract EAS19-1105

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**References**

1. Abdelhamid AS1, Martin N, Bridges C, Brainard JS, Wang X, Brown TJ, Hanson S, Jimoh OF, Ajabnoor SM, Deane KH, Song F, Hooper L. Polyunsaturated fatty acids for the primary and secondary prevention of cardiovascular disease. Cochrane Database Syst Rev 2018;11:CD012345.