NEWS EMBARGOED UNTIL 6PM LONDON TIME ON 4 AUGUST

The study will be published in the online journal Nature on 5 August

59 new genetic variants associated with blood cholesterol and triglyceride levels have been identified

- *Three of the genetic variants discovered, which are associated with HDL cholesterol, could be clear therapy targets for reducing the risk of myocardial infarction.*
- *The majority of the variants associated with LDL cholesterol that have been discovered are associated with a high risk of suffering a myocardial infarction*
- *The association between the genetic variants and the level of cholesterol and triglycerides does not show significant differences between European, Asian or Afro-American poopulations.*

Barcelona, 2 August 2010.- An international study which will be published in the next issue of the prestigious journal Nature, in which researchers from the IMIM (Hospital del Mar Research Institute) have participated, has identified 95 genetic variants related to LDL cholesterol, HDL cholesterol and triglyceride levels. Of these 95 associated genetic variants, 59 had not been previously identified. This discovery provides the biological basis needed to develop **a wider understanding of how the lipoprotein metabolism works and new therapy possibilities for preventing cardiovascular diseases are being identified.**

This project, in which researchers from 117 different institutions took part, carried out a whole genome association study on 100,184 people of European origin and on a further 35,000 people of non-European origin. In each participant 2,500,000 genetic variants were studied as well as the LDL colesterol, HDL colesterol and triglyceride levels. Later, the association between the genetic variants studied and the lipid parameters was analysed, identifying 95 genetic variants associated with one of the parameters analysed. According to Gavin Lucas, IMIM researcher and co-author of this work: "***The genetic variants identified explain between 10% and 12% of the variability of the different lipid parameters assessed. Furthermore, by working with such a broad sample, this study has enabled us to also study this association in relation to gender and geographical descent".***

One of the most important contributions of this project is the analysis carried out on the association of these genetic variants with myocardial infarction as, despite the

wide acceptance of the causal relationship between LDL cholesterol and infarction, the causal relationship between HDL cholesterol, triglycerides and myocardial infarction is very much debated. This debate was opened following the results of clinical tests using a drug which increases HDL cholesterol levels, but which does not reduce the risk of suffering a myocardial infarction. Nevertheless, this project has determined that, even though most of the genetic variants associated with HDL cholesterol that were studied did not support a causal relationship between HDL cholesterol levels and myocardial infarction, of the 27 genetic variants associated with HDL cholesterol only, two variants located in the *KLF14* and *C6orf106* genes were also associated with a higher risk of infarction; 1 variant, in the *NAT2* gene, of the 14 associated with triglyceride only, was associated with infarction; and 1 variant associated with HDL cholesterol and triglycerides, in the *IRS1* gene, was also associated with myocardial infarction. **This discovery is of great importance as it turns these genetic variants into key therapy targets for reducing the risk of suffering a myocardial infarction.**

The study has also established that the presence of these genetic variants **is associated with a higher risk of having extreme (very high) LDL cholesterol and triglyceride values and very low HDL cholesterol values**. We should bear in mind that LDL cholesterol is the one we commonly refer to as "bad cholesterol" since it is the one deposited onto the artery wall and which causes atherosclerosis. In contrast, HDL cholesterol, or "good cholesterol", transports this deposited cholesterol to the liver where it is eliminated.

"Whole genome association studies have opened up new research paths which enable us to learn about the genetic bases of different biological processes. Thanks to this study we now know more about the genetic bases which determine population-wide lipid levels and genetic variants are being identified which suggest new therapy targets for modifying triglyceride and HDL cholesterol levels, and thus reduce the risk of acute myocardial infarction, a disease affecting around 80,000 people per year in Spain and which is the main cause of death in developed countries" concludes Gavin Lucas.

Reference Article

(*) "Biological, Clinical, and Population Relevance of 95 Loci for Blood Lipids". DOI: 10.1038/nature09270
(*)Please see the attached document for the list of authors and institutions

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