Gyllensten, U; Guiducci, C; Groop, LC; Gonzalez, E; Gieger, C; Freimer, NB; Ferrucci, L; Erdmann, J; Elliott, P; Ejebe, KG; Döring, A; Dominiczak, AF; Demissie, S; Deloukas, P; de Geus, EJ; de Faire, U; Crawford, G; Collins, FS; Chen, YD; Caulfield, MJ; Campbell, H; Burtt, NP; Bonnycastle, LL; Boomsma, DI; Boekholdt, SM; Bergman, RN; Barroso, I; Bandinelli, S; Ballantyne, CM; Assimes, TL; Quertermous, T; Altshuler, D; Seielstad, M; Wong, TY; Tai, ES; Feranil, AB; Kuzawa, CW; Adair, LS; Taylor, HA; Borecky, IB; Gabriel, SB; Wilson, JG; Holm, H; Thorsteinsdottir, U; Gudnason, V; Krauss, RM; Mohlke, KL; Ordovas, JM; Munroe, PB; Kooper, JS; Tall, AR; Hegele, RA; Kastelein, JJ; Schadt, EE; Rotter, JI; Boerwinkle, E; Strachan, DP; Moores, V; Stefansson, K; Reilly, MP; Samani, NJ; Schunkert, H; Cupples, LA; Sandhu, MS; Ridker, PM; Rader, DJ; van Duijn, CM; Peltonen, L; Abecasis, GR; Boekholdt, SM; Kathiresan, S

Titel des Beitrags: Biological, clinical and population relevance of 95 loci for blood lipids.

Abstract: Plasma concentrations of total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglycerides are among the most important risk factors for coronary artery disease (CAD) and are targets for therapeutic intervention. We screened the genome for common variants associated with plasma lipids in >100,000 individuals of European ancestry. Here we report 95 significantly associated loci (P < 5 x 10^{-8}), with 59 showing genome-wide significant association with lipid traits for the first time. The newly reported associations include single nucleotide polymorphisms (SNPs) near known lipid regulators (for example, CYP7A1, NPC1L1 and SCARB1) as well as in scores of loci not previously implicated in lipoprotein metabolism. The 95 loci contribute not only to normal variation in lipid traits but also to extreme lipid phenotypes and have an impact on lipid traits in three non-European populations (East Asians, South Asians and African Americans). Our results identify several novel loci associated with plasma lipids that are also associated with CAD. Finally, we validated three of the novel genes-GALNT2, PPP1R3B and TTC39B-with experiments in mouse models. Taken together, our findings provide the foundation to develop a broader biological understanding of lipoprotein metabolism and to identify new therapeutic opportunities for the prevention of CAD.

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