Researchers find new genetic variants that put heavy drinkers at higher risk of liver cirrhosis

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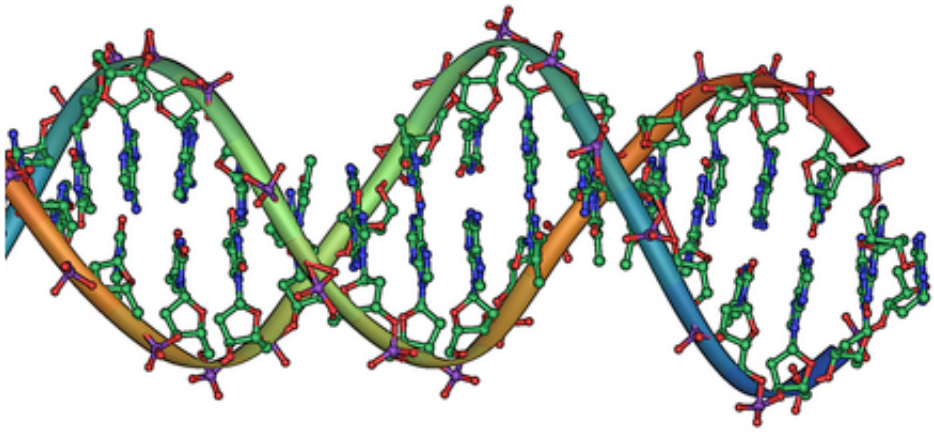

DNA double helix. Credit: public domain

(Medical Xpress)—A large team of researchers affiliated with multiple institutions in several European countries has found new genetic variants that put heavy drinkers at higher risk of developing cirrhosis of the liver. In their paper published in the journal *Nature Genetics*, the team describes their genome-wide association study of heavy drinkers that did and did not develop the disease and what they found in doing so.

Scientists know that most heavy drinkers develop an increase of fat in their livers, they also know that approximately 10 to 15 percent of heavy drinkers develop scarring of the liver—known as cirrhosis—which can lead to liver failure. What they'd like to better understand is why some heavy drinkers develop the disorder while others do not—to find out, they looked into the genes of a wide variety of heavy drinkers living in Germany, Belgium and the U.K. Such differences are obviously gene related, but until this study, just one genetic risk variant—in the gene PNPLA3—had been identified.

To learn more the researchers initially obtained genetic data on 410 heavy drinkers living in Germany that had developed cirrhosis and on 1,119 heavy drinkers that did not. They then obtained the same type of information for people living in Belgium and the U.K. Next, they conducted genetic imputation using the data they had obtained with information found in the 1000 Genomes Project and IMPUTE2. That allowed them to isolate differences between the two groups of heavy drinkers, and not only confirmed the variant in the PNPLA3 gene, but revealed two more, one in the MBOAT7 gene and the other in the TM6SF2 gene—all three of the genes involved, the team notes have been previously identified as important in the processing of fats, and now it appears that they are linked to cirrhosis as well.

Isolating the genes responsible for putting heavy drinkers at increased risk of cirrhosis, the researchers note can help to single out those drinkers who are most at risk so that measures can be taken before serious damage can occur. It also might help in developing a means for preventing it from happening in the first place.

More information: Stephan Buch et al. A genome-wide association study confirms PNPLA3 and identifies TM6SF2 and MBOAT7 as risk loci for alcohol-related cirrhosis, *Nature Genetics* (2015). DOI: 10.1038/ng.3417

Abstract

Alcohol misuse is the leading cause of cirrhosis and the second most common indication for liver transplantation in the Western world. We performed a genome-wide association study for alcohol-related cirrhosis in individuals of European descent (712 cases and 1,426 controls) with subsequent validation in two independent European cohorts (1,148 cases and 922 controls). We identified variants in the MBOAT7 ($P = 1.03 \times 10{-}9$) and TM6SF2 ($P = 7.89 \times 10{-}10$) genes as new risk loci and confirmed rs738409 in PNPLA3 as an important risk locus for alcohol-related cirrhosis ($P = 1.54 \times 10{-}48$) at a genome-wide level of significance. These three loci have a role in lipid processing, suggesting that lipid turnover is important in the pathogenesis of alcohol-related cirrhosis.

Press release