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Gene discovery linked to alcohol-induced liver disease

The findings of an international study led by the Centenary Institute suggests that the possibility of high-risk drinkers developing alcohol-induced cirrhosis is in part related to genetic factors.

“Only a small proportion of high-risk drinkers, about 15 percent, actually develop cirrhosis but those who do are at high risk of death and require substantial health-care support,” said senior author of the published study Clinical Associate Professor Devanshi Seth, Head of the Centenary Institute Alcoholic Liver Disease Research Program and also affiliated with Drug Health Services, Royal Prince Alfred Hospital, Sydney Local Health District.

“We wanted to see if certain high-risk drinkers had a genetic predisposition for alcohol-induced cirrhosis. High-risk drinking is chronic alcohol use above recommended guidelines,” said Clinical Associate Professor Seth, the senior author of the study.

Reported in the science journal ‘Hepatology’ the study was undertaken by a multi-national GenomALC Consortium involving the Southern California Institute for Research and Education (SCIRE) and other research collaborators.

Identified by the study researchers is a new gene associated with alcohol-induced cirrhosis. The novel FAF2 gene is associated with a reduced cirrhosis risk for heavy drinkers. Also confirmed by the study were four additional genes, three previously found to be associated with an increased risk and one with reduced risk of cirrhosis in heavy drinkers.

“Interestingly, a commonality of these genes, including the novel FAF2, is that they appear to affect the lipid (fat) metabolism pathway,” said Clinical Associate Professor Seth.

“The findings are important as due to heavy drinking, it is the build-up of lipid droplets in the liver, that can cause inflammation, and which may then lead to serious liver complications such as cirrhosis in some drinkers,” she said.

The researchers believe that the identified genes are influencing the body’s ability to regulate lipid droplets in the liver and are therefore influencing cirrhosis risk levels.

“This new understanding opens the door to the future development of exciting new drug treatments that can potentially target these specific genes and lipid processes, and reduce the chances of at-risk individuals contracting this devastating disease,” said Dr Timothy Morgan, co-senior author of the study and researcher at the SCIRE.

Clinical Associate Professor Seth says, “Abstaining or reducing alcohol use remains the most effective treatment, however fully understanding the genetic mechanics of alcohol-induced cirrhosis is also key to improving patient diagnosis and treatment decisions.”

“Identifying these genes at an individual level, in combination with assessing lifestyle options, means that we will now be able to predict an individual’s risk profile and then better personalise an appropriate treatment response,” she said.

The research was funded by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) a part of the National Institutes of Health (NIH), USA.

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Publication:

Genome-wide association study and meta-analysis on alcohol-related liver cirrhosis identifies novel genetic risk factors.

<https://aasldpubs.onlinelibrary.wiley.com/doi/10.1002/hep.31535>

Images:

Clinical Associate Professor Devanshi Seth, Centenary Institute:

<https://drive.google.com/file/d/1m0K6G4D52gtKuYFdhpuu-yrB8lejRnzM/view?usp=sharing>

Drinking alcohol (2 images):

<https://drive.google.com/file/d/1v-y5NcqZ9G99gi8Lr6FqgoGelx0dOcd3/view?usp=sharing>

<https://drive.google.com/file/d/10DKh7S3QLixGthBgb1IcS1e52236EUZe/view?usp=sharing>

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About the Centenary Institute

The Centenary Institute is a world-leading independent medical research institute, closely affiliated to the University of Sydney and the Royal Prince Alfred Hospital. Our research focuses on three key areas: cancer, inflammation and cardiovascular disease. Our strength lies in uncovering disease mechanisms and applying this knowledge to improve diagnostics and treatments for patients.

For more information about the Centenary Institute, visit www.centenary.org.au

About the GenomALC Consortium

The GenomALC Consortium is a collaboration between a number of research groups worldwide who are contributing data collected on individuals who are alcohol dependent, with the aim of gaining a better understanding of the genetic effects involved in the development of liver diseases.

For more information about the GenomALC Consortium, visit <https://genomalc.org/>