Genes modify the risk of liver disease among alcoholics

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It has been widely observed that only a small percentage of alcoholics develop cirrhosis of the liver, the most advanced form of alcoholic liver disease (ALD); the reason why all alcoholics do not develop such disease is not known. The present study from Spain, that includes original work and a meta-analysis, evaluates whether genetic polymorphisms that determine levels of glutathione-S-transferases (GST) relate to the risk of developing ALD among alcoholics. Alcoholics with certain genetic GST polymorphisms were found to be at significant excess risk for such liver disease in comparison with alcoholics without these polymorphisms.

As stated by the authors, the theory that these enzymes may affect risk is based on the ability of certain GST alleles to detoxify harmful ethanol metabolites in the liver by conjugating acetaldehyde and ROS to reduced glutathione. The specific polymorphisms that the authors found to be associated with increased liver disease are among those that would be expected to lower the activity of the corresponding GST enzymes; this would permit higher levels of toxic metabolites of alcohol and oxidative stress to be present for longer periods of time after excessive alcohol consumption.

Some Forum reviewers thought that while the study was well done, the authors were unclear how these data could directly lead to "potential therapeutic targets" for liver disease in alcoholics. Nevertheless, the original study and meta-analysis provide important data on how specific genetic factors relate to the development of liver disease among alcoholics and could theoretically lead to better strategies for the

prevention and treatment of alcoholic liver disease.

More information: Marcos M, Pastor I, Chamorro A-J, Ciria-Abad S, González-Sarmiento R, Laso F-J. Meta-analysis: glutathione-S-transferase allelic variants are associated with alcoholic liver disease. *Aliment Pharmacol Ther* 2011;34:1159.

For the detailed critique of this paper by the International Scientific Forum on Alcohol Research, go to www.bu.edu/alcohol-forum or www.bu.edu/alcohol-forum/criti … ics-5-december-2011/

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