Gout medications might be useful in treating alcohol-induced liver disease

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New research in mice shows that two commonly used gout medications, which target uric acid and adenosine triphosphate, may offer protection from alcohol-induced liver disease and inflammation. These findings suggest that clinical trials in humans with alcoholic liver disease should be considered. The report appears in the August 2015 issue of the *Journal of Leukocyte Biology*.

"This study should ultimately help patients with alcoholic liver disease to prevent and/or treat acute episodes of alcoholic hepatitis, a potentially lethal condition," said Gyongyi Szabo, M.D., Ph.D., a researcher involved in the work from the Department of Medicine at the University of Massachusetts Medical School in Worcester, Massachusetts.

To make this discovery, Szabo and colleagues used immune cells from human volunteers as well as four groups of mice. In the human cell experiments, immune cells were isolated and exposed to alcohol-treated human hepatocytes in a test tube. Results indicated that uric acid and ATP, components released from alcohol-damaged hepatocytes, activated the inflammasome, a component of the innate immune system. In the mouse experiments, the first group consisted of wild-type (i.e. "normal") mice and the second were mice deficient in the NLRP3 inflammasome component. Both groups received chronic alcohol-containing diet. The third group consisted of wild-type (i.e. "normal") and the fourth NLRP3 deficient mice; both of these groups received control alcohol-free diet. Of those that were on the chronic alcohol diet, the wild-type mice, but not the NLRP3-deficient mice developed characteristics of alcoholic

liver disease. Liver damage induced by alcohol was associated with increases in the circulating levels of sterile danger molecules, uric acid and ATP. None of the mice on a control (non-alcohol) diet developed any symptoms of alcohol-related liver disease.

"We are increasingly appreciating the central role of inflammation and immune responses in a variety of diverse diseases," said John Wherry, Ph.D., Deputy Editor of the *Journal of Leukocyte Biology*. "The link between alcohol induced tissue damage and sensing by the immune system through the inflammasome opens the door for new therapeutics targeting this type of inflammation in liver diseases."

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