

Public Abstract

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Title:HISTONE H3 PHOSPHORYLATION AND PHOSPHOACETYLATION IN THE LIVER OF RATS TREATED IN VIVO WITH ACUTE ETHANOL

Overindulgence of ethanol leads to alcoholic liver disease characterized by hepatitis (inflammation), steatosis (fatty liver) and cirrhosis (fibrosis). Alcoholic liver disease can also progress to hepatocellular carcinoma (liver cancer) and in some cases death, especially for the chronic abusers. Despite this, there is no FDA approved drug for treating this problem. Binge drinking is on the rise and binge drinkers are more susceptible to alcohol induced injury over a shorter time. The mechanisms of the effects of alcohol on liver injury are not completely understood. Ethanol is known to affect the expression of genes. The relevance of DNA-binding proteins called histone is gaining more light in the effects of alcohol on the liver. Modifications of these proteins are known to increase and decrease the expression of genes by allowing or preventing access to the DNA. In this context, we utilized an acute model where rats were administered ethanol intraperitoneally, to mimic the effects seen in binge drinking in humans. We achieved blood ethanol levels similar to those seen in human binge patients. We also observed liver injury i.e. apoptosis, necrosis and steatosis. Binge administration of ethanol promoted the phosphorylation of serine 10 and 28, as well as the phosphoacetylation (lysine 9/Serine 10) of histone H3. Phosphorylation was associated with the promoters of the genes c-Fos and c-Jun (serine-10), c-Jun and PAI-1 (serine-28) and phosphoacetylation with PAI-1. C-Fos, c-Jun, and PAI-1 have been implicated in alcoholic liver injury. This study demonstrate for the first time that ethanol binge induction of histone H3 phosphorylation and phosphoacetylation in vivo in liver is associated with the promoters of genes involved in alcoholic injury, and offers a new molecular mechanism for the actions of ethanol in liver.