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"Differential expression of cardiac fibrosis genes in response to chronic and binge alcohol consumption in male C57BL6/J mice"

According to the National Institute on Alcohol Abuse and Alcoholism (NIAAA), over 172 million American adults reported alcohol consumption and 60.3 million US adults reported binge drinking in 2022. The NIAAA defines binge drinking as a pattern that raises the blood alcohol concentration (BAC) to at least 0.08% within two hours. Binge drinking can cause permanent injury to many tissues in the body, such as the liver and the gastrointestinal, pulmonary, and cardiovascular systems, and the cardiac effects of chronic alcohol consumption on the heart can be severe. Alcohol-induced cardiomyopathy (ACM) is a leading cause of non-ischemic dilated cardiomyopathy, which is characterized by both systolic and diastolic failure. Prior to systolic dysfunction, chronic alcohol use causes fibrosis and diastolic dysfunction in the heart. However, there are few studies on the regulation of the fibrotic process in ACM. By isolating RNA taken from mice hearts affected with ACM, we studied the differential expression of various genes associated with cardiac fibrosis. We hypothesized that hearts from mice exposed to chronic and binge ethanol feeding would have greater expression of fibrosis-related genes.

Male C57BL6/J mice were fed the Lieber-Decarli liquid diet for 30 days with or without 5% ethanol. In addition to the chronic 30-day feeding, the mice were given binges by oral gavage on days 10 and 30. The ethanol-exposed mice were given a binge ethanol dose of 5 g/kg, while the control mice were given a gavage of isocaloric maltose dextrin. On day 32, 48 hours after the second gavage feeding, the mice were sacrificed, and hearts were collected. RNA was isolated from the left ventricle and sent for sequencing. RNA expression was then used to study the regulation of cardiac fibrosis in our preclinical model of ACM.

After analyzing the RNAseq data from alcohol-exposed mice hearts, we saw that multiple genes involved in cardiac fibrosis had altered expression. Cellular communication network factor 2 (CCN2) was one gene significantly upregulated in the alcohol group. CCN2 is involved in the TGF-β pathway to promote remodeling of the extracellular matrix and fibrogenesis. C/EBPδ, an upstream activator of CCN2, was another gene with increased expression and ultimately leads to cardiac fibrosis. Chemokine ligand 2 (CCL2) was also upregulated and is a proinflammatory chemokine that recruits monocytes to release TGF-β, which activates cardiac fibroblasts. The upregulation of these genes reveals part of the underlying molecular pathways responsible for the development of cardiac fibrosis in ACM.