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"The Role of TRAF3IP2 in the Progression of Alcoholic Cardiomyopathy"

Alcoholic Cardiomyopathy (ACM) manifests in humans after excessive alcohol consumption and is characterized by ventricular dilation and cardiac function impairment. Previous studies have identified deterioration of mitochondrial homeostasis, increased oxidative stress, and inflammation as mechanisms of ACM development. However, little is known of the molecular mechanism of ACM. Here, we focus on the role of TRAF3IP2, a proinflammatory cytoplasmic adapter protein, in the pathogenesis of ACM. Previous work suggests TRAF3IP2 is a master regulator of inflammation; thus, being a potential therapeutic target. In this study, we used a mouse model of chronic plus binge alcohol feeding described by the NIAAA. After 5 days of acclimation to the liquid diet, mice are fed *ad libitum* 5% ethanol (EtOH) liquid diet (Lieber-DeCarli) or isocaloric control liquid diet for either 10 days or 20 days. At days 10 and 20, mice received an oral binge dose of EtOH (5 g/kg body wt), or isocaloric maltose dextrin solution (9 g/kg body wt), via oral gavage. Ethanol plasma levels are expected to reach 180 mg/dl following the 10d ethanol feeding and increase to 400 mg/dl for 2 hours. Mice are given at least 9 hours after binge before cardiac measurements are performed to avoid the acute cardiac effects of EtOH intoxication. Echocardiography is performed at baseline and following binges to assess *in vivo* cardiac structure, function, and disease progression. After either 10 days or 20 days, left ventricular function was assessed via catheterization with a pressure-volume conductance catheter. The heart was dissected, and the left ventricle was isolated and split for RNA and protein assays. The liver and other tissues were collected for future use. qPCR was performed for TRAF3IP2, other inflammatory markers (IL-1β, IL-6, TGFβ), and fibrosis markers (Col I, Col III, LOX). qPCR results show no significant difference between control and ethanol fed mice at 10 days and 20 days for TRAF3IP2, IL-1β, IL-6, TGFβ, Col I, Col III, and LOX. LARP6 was increased in ethanol fed mice at 10 days when compared to control mice ($P=0.035$) while no significant difference in LARP6 expression occurred after 20 days. Cardiac function as determined by echocardiogram shows increased ejection fraction in 10 day ethanol mice ($P<0.05$). All other cardiac parameters were unchanged for the 10 day and 20 day cohort. Further studies with increased sample sizes are needed to uncover the molecular mechanisms of ACM.