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"Impact of Chronic Binge Alcohol on Hepatic Immune Infiltration in SIV-Infected Rhesus Macaques"

BACKGROUND: Liver disease is a leading cause of death in individuals with HIV, particularly among those who misuse alcohol. Chronic alcohol use and SIV/HIV infection disrupt liver immune regulation, leading to hepatocyte injury and inflammation. While T cells, like CD4+ and CD8+, play a role in liver pathology, the broader contribution of adaptive immune cells and inflammatory cytokines in alcohol-related liver disease remains understudied. Chronic alcohol and HIV exposure increase pro-inflammatory Th1 CD4+ T cells and cytokines such as IFN-γ and TNF-α, which are hepatotoxic. Furthermore, alterations in the balance of proinflammatory to anti-inflammatory cytokines, like IL-10, from combined alcohol misuse and HIV infection may additionally contribute to liver pathology. Therefore, we hypothesize that chronic binge alcohol will increase immune cell infiltration and inflammation in a model of SIV infected rhesus macaques.

OBJECTIVES: This preliminary study aims to identify the contribution of alcohol to immune cell infiltration and inflammation in the livers of SIV-infected rhesus macaques and its role in the progression of alcohol-related liver disease.

METHODS: Female rhesus macaques received either chronic binge alcohol or vehicle control (water) for 14 months via infusion pumps. After 3 months, all animals were intravaginally infected with SIVmac251. Antiretroviral therapy was initiated 2.5 months post-infection and continued for 9 months. At study endpoint, liver tissue was collected and homogenized for RNA extraction. RNA was reverse transcribed to cDNA, then SYBR-based qPCR was conducted to quantify gene expression and mRNA levels were normalized to RPS13.

RESULTS: A significant decrease in IL-10 mRNA expression was observed in CBA-treated macaques compared to vehicle controls, suggesting reduced anti-inflammatory signaling. No significant differences were detected in expression of IL-1β, TNF-α, IFN-γ, IFN-γ receptor, CD4, CD8, or the CD4/CD8 ratio. We will further examine additional inflammatory markers including CD38 (immune cell activation), CD25 (Tregs), MCP-1 (monocyte recruitment), CXCR4 and CCR5 (chemokine receptors involved in inflammation and SIV targeting).

CONCLUSIONS: Preliminary findings of diminished IL-10 may indicate an early shift of anti-inflammatory to pro-inflammatory signaling in the liver. Future directions may include evaluating additional acute markers of liver damage and considering the addition of dietary or metabolic stressors to enhance liver disease progression modeling. These studies will help elucidate how immune cell signaling contributes to the development and progression of alcohol-associated liver disease in people living with HIV.