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Chronic Binge Alcohol Increases Susceptibility to Rectal SIV Infection in Macaques

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Several studies have identified alcohol abuse as a risk factor for HIV transmission, suggesting a synergistic interaction between these two major public health concerns [1–3]. Among people living with HIV/AIDS, alcohol use has also been clearly associated with risky sexual behavior [4]. Alcohol abuse is prevalent in many areas of the world with large populations of HIV-infected patients, and among those living with HIV in the United States, alcohol abuse rates are nearly twice those of the general population [5, 6]. While this risky behavior increases risk for HIV transmission, it is not clear as to how alcohol may affect host biological factors and contribute to virus transmission. Studies have associated alcohol abuse with impairment of host defenses and increased susceptibility to disease [7]. Taken together, these observations provide evidence that alcohol abuse may alter host innate defense mechanisms, thus facilitating virus transmission and early replication in a newly infected host. Utilizing the SIV-infected rhesus macaque exposed to chronic binge alcohol consumption (CBA), we have identified increased plasma SIV levels at set-point and an accelerated disease course in CBA animals relative to sucrose-treated controls [8, 9]. Additionally, macaque studies have identified alterations in immune cells in the periphery and gut mucosa [10, 11].

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Author Contribution

All of the authors were involved in the design and implementation the studies, and have reviewed and edited the letter. AMA, RV and GJB analyzed the data and drafted the letter.

Conflicts of Interest

We declare there are no conflicts of interest.

Our recent pathogenesis studies have utilized both male (n = 27) and female (n=16) rhesus macaques exposed to either daily intoxicating doses of ethanol (to achieve 50mM blood alcohol) or isocaloric sucrose (SUC) via a gastric catheter. Following 3 months of daily exposure, animals were intra-rectally inoculated with 250 TCID₅₀ of SIV_{MAC}

These results highlight the need for additional studies to further examine the innate immune parameters in the rectal mucosa affected by CBA and to determine their influence on early host interactions with HIV/SIV. Although relatively little information is known about the impact of alcohol on the rectal mucosa, alcohol use has been shown to affect the integrity of the epithelial barrier of the gut, resulting in increased microbial translocation and inflammatory responses [15]. Additionally, previous studies in alcohol-treated macaques have identified an increased percentage of SIV target cells in duodenum of alcohol-treated macaques as compared to controls after 3 months of chronic exposure [11]. We hypothesize that similar alterations to the mucosal epithelial barrier and immune cells of the lower colon and rectum would facilitate SIV/HIV acquisition and early replication.

The marked difference observed in female infection rates also warrant additional studies to examine sex-specific factors that may influence transmission, including hormonal fluctuations. Previous studies have associated susceptibility to vaginal infection of macaques with higher progesterone levels; however, at the time of rectal inoculation in our study, 3 of the females that resisted infection were in the secretory phase of the cycle when progesterone levels would be highest. Further studies that evaluate how CBA consumption affects vaginal transmission of SIV/HIV are needed to evaluate susceptibility to vaginal transmission, as this represents the predominate route of infection in females.

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Figure 1.

Infection rates in rhesus macaques following intra-rectal (IR) and intravenous (IV) exposure to 250 TCID₅₀ of SIV_{MAC251}. Animals were given daily doses of ethanol (CBA) to achieve 50mM blood alcohol levels or isocaloric amounts of sucrose (SUC) via gastric catheters, beginning 3 months prior to the first virus challenge. Kaplan-Meier plots of infection rates were generated and compared using log-rank statistics (Mantel-Cox) in *Prism* version 5 (GraphPad Software, INC., La Jolla, CA) **A.** Infection rate in 14 CBA males and 13 SUC controls (p=0.06). **B.** Infection rate in 8 CBA females and 8 sucrose controls (p=0.025).