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"Chronic Binge Alcohol Administration Increases $CD8^+$ T Cell Immunosenescence in Female Rhesus Macaques"

Background: Aging is accelerated by HIV and by alcohol use. Aging is associated with cellular senescence, which is permanent proliferative arrest, and occurs in response to endogenous and exogenous stresses. In the immune system, aging is associated with immunosenescence, during which both innate and adaptive immune systems lose the ability to respond to antigen but produces large quantities of pro-inflammatory mediators. The immunopathy associated with HIV infection has been suggested to accelerate immunosenescence through chronic persistent inflammation. At-risk alcohol use is twice as likely in persons with HIV (PWH) compared to the general population, and the percentage of women with alcohol use disorder (AUD) increased 83.7% from 2002-2012. Previous work has found that chronic binge alcohol (CBA) and AUD augment CD8+ T cell activation and immunosenescence in SIV-infected male macaques and PWH.

Hypothesis: CBA-administered female rhesus macaques have higher frequency and total senescent CD8+ T cells than vehicle-administered female macaques.

Methods: Adult SIV-infected female rhesus macaques received alcohol intragastrically for 14.5 months. Three months into either vehicle (VEH) or CBA treatment, blood was collected, and PBMCs were isolated, counted, and cryopreserved at -80°C. Four markers were used to define senescent cells: loss of CD28 was used as a senescent marker, CD38 marked activated cells, and Ki-76 and Tag-It were used to define proliferating cells. Identification and percentage of senescent cells were determined using a BD LSR II flow cytometer and DIVA version 10.8.1.

Results: Paired T-tests for CBA animals showed a trend ($p=0.13$) toward more CD8+CD28- T cells than CD8+CD28+ cells, while VEH animals trended toward more CD8+CD28+ than CD8+CD28- T cells. Unpaired T-test found that CBA animals trended ($p=0.19$) toward a higher CD28-/CD28+ ratio within the CD8+ T cell population compared with VEH animals.

Conclusions: Our results suggest that 3 months of CBA administration potentially increases senescent $CD8^+$ T cells in rhesus macaques. The inflammatory immune environment associated with increased senescent $CD8^+$ T cells could make animals more susceptible to SIV infection. Future studies will determine the effect of CBA administration on $CD8^+$ T cell senescence in SIV-infected and ovariectomized female macaques. (Supported by LIST GRANTS)