Increased Immune Activation after Gut Permeabilization in SIV-Infected AGMs

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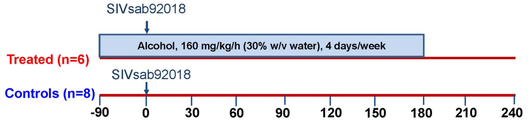
Background: Microbial translocation (MT) has been proposed as a major cause of increased immune activation in HIV/SIV infection and subsequent cardiovascular comorbidities, including hypercoagulability.

Hypothesis: Alcohol administration to African green monkeys (that maintain a healthy intestinal barrier despite high levels of viral replication during chronic SIV infection) will result in increased gut permeability and consequent levels of immune activation and hypercoagulability.

Design: Chronic alcohol administration to 6 AGMs via indwelling gastric catheters for 3 months, followed by SIVsab92018 infection and 240 days follow-up. Alcohol was discontinued at 180 days postinfection to assess the resolution of the effects of alcohol administration.

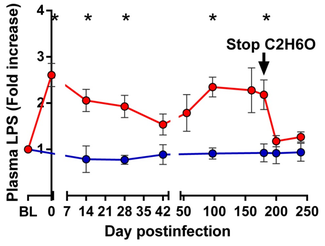
Control group was formed by 8 AGMs that were IV-challenged with SIVsab92018, in which infection followed its natural course.



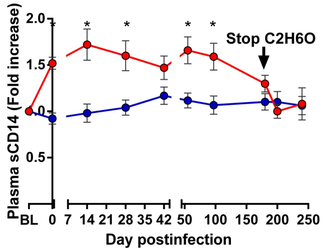
Methods: Assessment of the levels of MT (LPS, sCD14), T cell changes, immune activation (HLA-DR CD38 and Ki-67), coagulation (D-Dimer), plasma cytokines and viral replication in alcohol-treated infected AGMs and infected AGM controls. Microbial products and fibrosis were assessed in the liver by immunohistochemistry.

Alcohol administration to AGMs altered the mucosal barrier and resulted in increased microbial translocation.

LPS

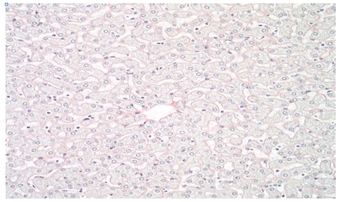


sCD14

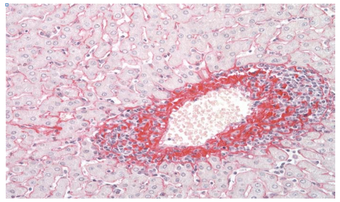


Impact of alcohol administration on the liver (collagen)

Control

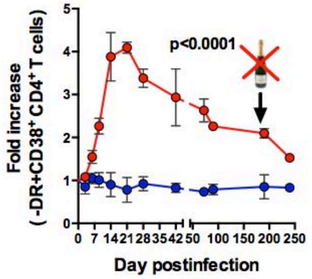


Alcohol-treated

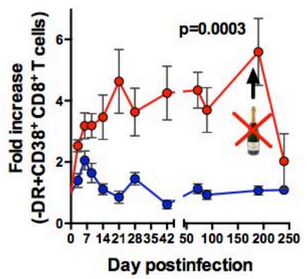


Induction of MT during acute SIVsab infection of AGMs significantly impacted T cell activation.

CD4+ T cell activation

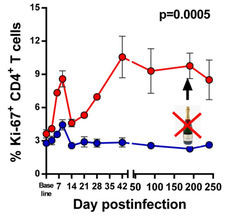


CD8+ T cell activation

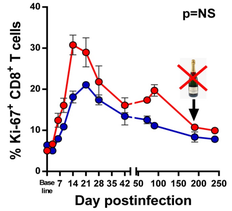


Induction of MT during acute SIVagm infection of AGMs significantly impacted T cell proliferation…

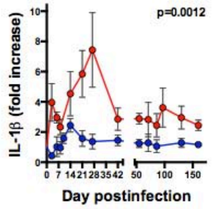
CD4+ T cell proliferation

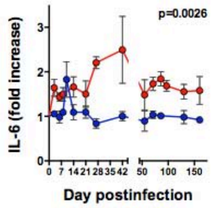


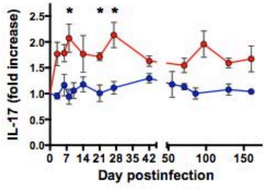
CD8+ T cell proliferation

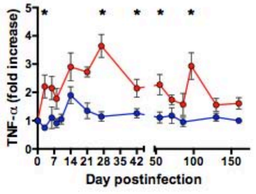


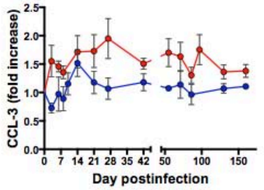
…and the dynamics of inflammatory cytokines and chemokines.

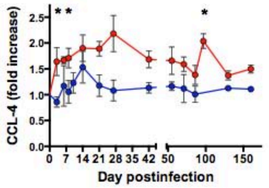




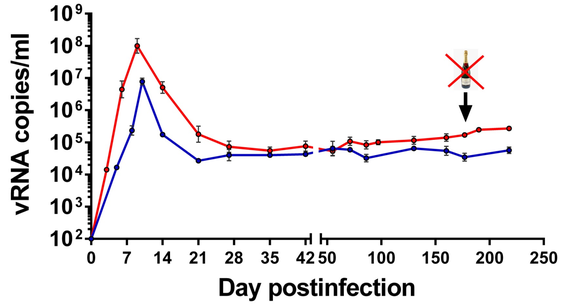






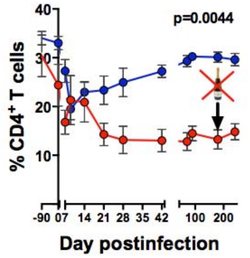


Slight increase in plasma VLs

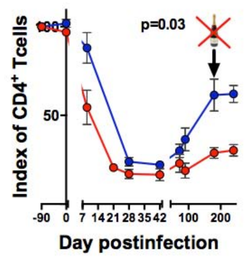


Delayed CD4+ T cell restoration in the gut and periphery

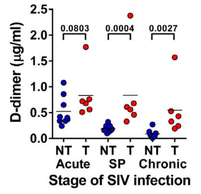
Peripheral CD4+ T cell (%)



Mucosal CD4+ T cells



Significant impact on coagulation



Conclusions

- We confirmed that alcohol plays a role in permeabilizing the gut and increases microbial translocation in this non-human primate model that maintains gut integrity during SIV infection.
- Alcohol treatment of SIVagm-infected AGMs resulted in increased systemic immune activation and inflammation, delayed immune restoration, and activation of coagulation.