339

Sustained inflammation and delayed resolution of COVID-19 disease in immunocompromised SIV infected macaques

Dhiraj K. Singh[1,2] *, Gayathri Ravichandran[1,2], Garima Arora[1,2], Xavier Alvarez[1,2], Ricardo Carrion[1,2], Shannan Hall-Ursone[1,2], Edward Dick[1,2], Deepak Kaushal[1,2]
[1]Southwest National Primate Research Center, [2]Texas Biomedical Research Institute, San Antonio, TX 78245, USA.

BACKGROUND

Background: COVID-19 continues to be a health challenge with critical knowledge gaps existing in the understanding of mechanisms driving severity in comorbid conditions. Clinical observations points to a higher susceptibility to COVID-19 in people living with HIV (PLHIV) but the precise mechanisms are still unknown.

METHODS

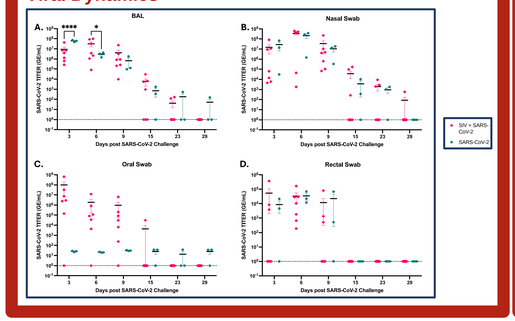
Our group was amongst few that established the rhesus macaque model of COVID-19 infection early on during the pandemic. We are now leveraging this established NHP model of COVID-19 with the long-standing, highly validated, pathogenic AIDS NHP model to study a central hypothesis that underlying SIV infection and the resulting immune activation promotes severity of COVID-19 presentation by profiling the dynamics of viral titers (measured via molecular virology), induced tissue pathology (measured via live PET/CT imaging and conventional histopathology), and underlying immunological perturbations (measured via flow cytometry and single cell transcriptomics).

RESULTS

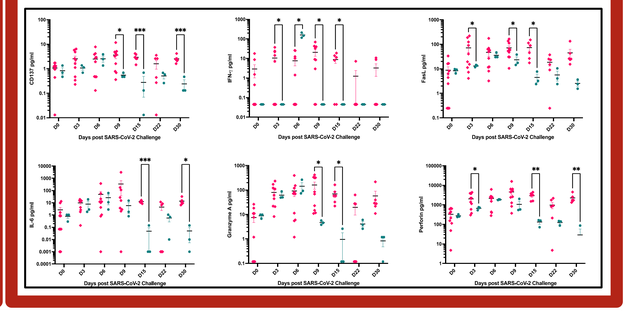
Macaques infected with SIV develop acute immunodeficiency within 2-4 weeks and progress to chronic AIDS over 5-6 months. When infected with SARS-CoV-2 these macaques develop mild-to-moderate COVID-19 with an extended acute hyperinflammatory state. Co-infected macaques demonstrate higher etiology of either diseases, enhanced lung and brain involvement as measured by PET/CT. Post SARS-CoV-2 infection in SIV coinfected macaque, the F-18 FDG uptake increased in lymph nodes, brain and gut during the acute phase followed by a decline in the post-acute phase. Investigations of the underlying specific immune mechanisms revealed perturbations in the airway myeloid cell composition, T cell phenotypes, activation status and antigenic responsiveness.

COVID-19 in SIV co-infected macaques is characterized by extended acute hyperinflammatory phase and delayed resolution of disease.

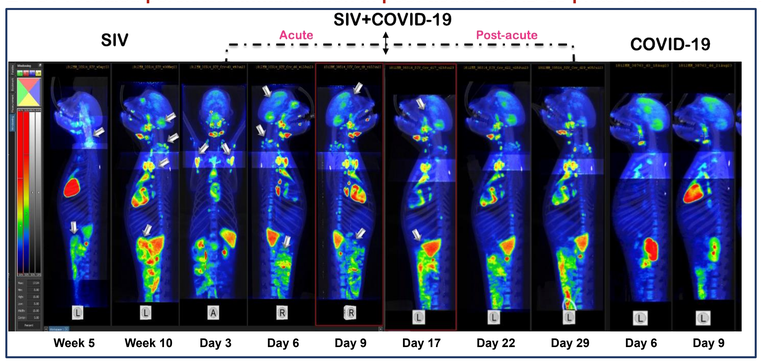
Viral Dynamics



Alveolar cytokine storm persists longer in SIV coinfected NHPs.



18F-FDG PET-CT revealed persistent inflammation in post-acute COVID-19 phase of coinfected macaques.



CONCLUSIONS

- **The pathogenesis and resolution of SARS-CoV-2 induced COVID-19 is modulated by an underlying SIV coinfection in NHPs.**
- **Peak viral titers was observed on Day 6 post-SARS-CoV-2 challenge in lower respiratory tract (BAL fluid) of co-infected macaques while macaques infected with SARS-CoV-2 exhibit peak viral titers on Day 3 post-SARS-CoV-2 challenge.**
- **Alveolar cytokine storm persists longer in SIV coinfected NHPs.**
- **18-F FDG uptake increases in lymph nodes, brain and gut during the acute phase showing a peak on Day 6 post SARS-CoV-2 infection followed by a decline in the post-acute phase. 18F-FDG PET-CT revealed persistent inflammation in post-acute COVID-19 phase of coinfected macaques.**

ACKNOWLEDGEMENTS

The work described in this poster was supported by NIH award # R01 AI 170197 and COVID-19 research grant from San Antonio Medical Foundation to D.K.S and by institutional NIH awards P51OD111033 and U42OD010442 to the SNPRC, Texas Biomedical Research Institute.

CONTACT INFORMATION

Dhiraj Kumar Singh, Ph.D.
Staff Scientist II
Southwest National Primate Research Center
Texas Biomedical Research Institute
dsingh@txbiomed.org