00200

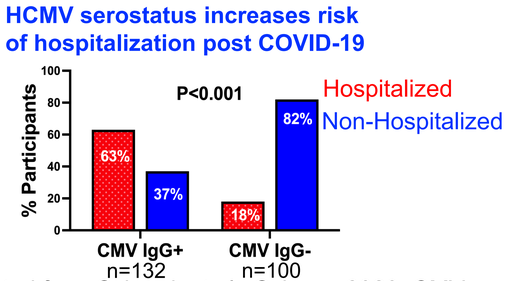
Pulmonary CMV Reactivation Following SARS-CoV-2: Implications for Immunopathology

Jamin W. Roh[1,2], Peter A. Barry[2,3], Peter W. Hunt[4], Smita S. Iyer[2,3]

[1] Graduate Group in Immunology at UC Davis, Davis, California, USA [2]Center for Immunology and Infectious Diseases, Davis, California, USA [3]California National Primate Research Center, Davis, California, USA [4]Division of Experimental Medicine UC San Francisco, San Francisco, California, USA

BACKGROUND

SARS-CoV-2 infection results in a spectrum of disease severity attributable to the magnitude of the underlying inflammatory response. Aged individuals with co-morbidities are most vulnerable and severely affected, but the mechanisms driving aberrant immune responses fueling SARS-CoV-2 immunopathology in this high-risk population are not fully elucidated. We hypothesized that asymptomatic cytomegalovirus (CMV) infection might exacerbate SARS-CoV-2 pathogenesis since its replication is both a cause and consequence of inflammation and appears to worsen oxygenation in critically ill patients (Limaye, JAMA, 2017). CMV-seropositivity was associated with increased hospitalization among people with SARS-CoV-2 infection (Shrock, Science, 2020; Figure A).

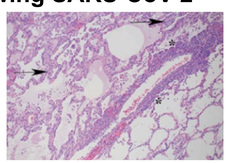


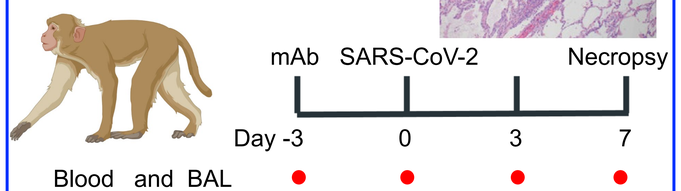
(A) Data adapted from Schrock et al., Science 2020, CMV seropositivity is correlated with increased risk of hospitalization compared to seronegative individuals.

METHODS

Hypothesis: CMV is reactivated following SARS-CoV-2 infection

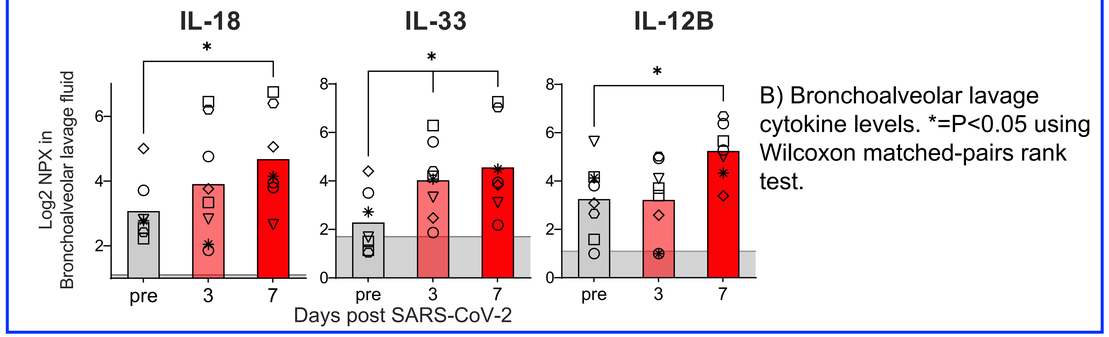
♀ Aged:18-23 years Treatment (T) : n=4 Control (C) : n=4



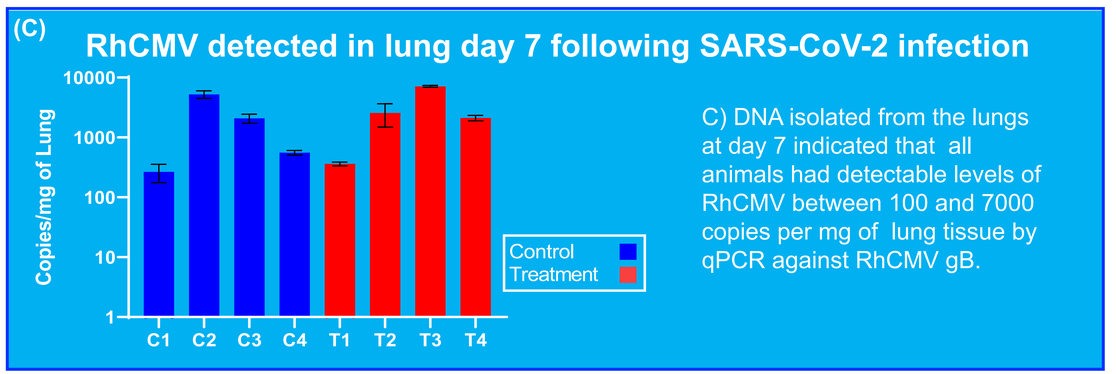


- 8 female rhesus macaques with type 2 diabetes, aged 18-23 years naturally infected with Rhesus (Rh) CMV were infected with SARS-CoV-2 ($2.5x10^6$ PFU) and monitored for 7 days.
- Animals were given either SARS-CoV-2 neutralizing monoclonal antibodies or control antibodies
- Lung, liver, ileum, and colon were collected at necropsy. Blood was sampled pre infection, day 3, and day 7

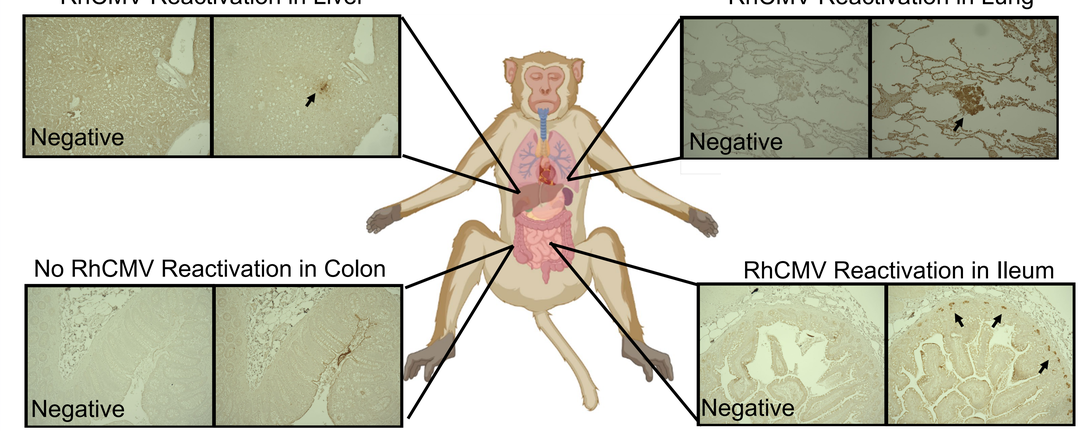
RESULTS



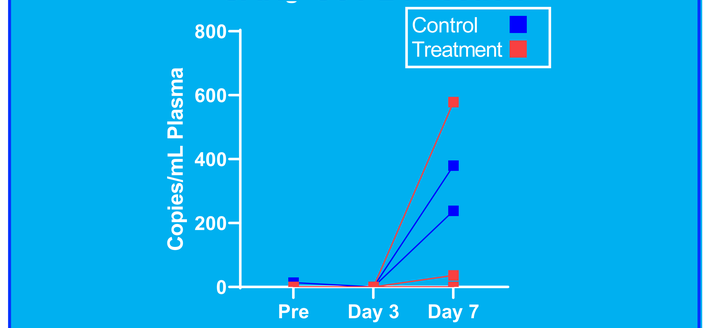
B) Bronchoalveolar lavage cytokine levels. *=P<0.05 using Wilcoxon matched-pairs rank test.



C) DNA isolated from the lungs at day 7 indicated that all animals had detectable levels of RhCMV between 100 and 7000 copies per mg of lung tissue by qPCR against RhCMV gB.



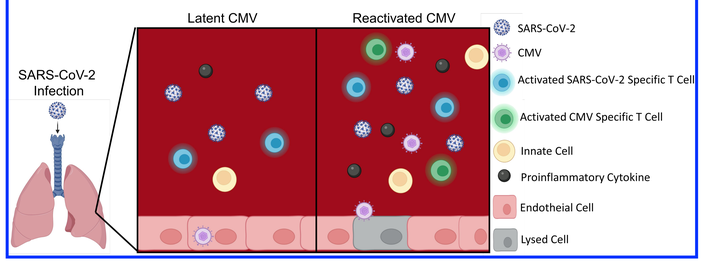
D) RhCMV IE1 staining following 7 days of SARS CoV-2 infection. Black arrows indicate positively stained sections Images are 10x magnification. Negative indicates slide not stained with primary antibody.



E) In plasma RhCMV was detected (above limit of detection) in 4 out of 8 animals following SARS-CoV-2 infection

CONCLUSIONS

SARS-CoV-2 infection of RhCMV-seropositive macaques results in CMV reactivation in the anatomic sites where SARS-CoV-2 causes pathology as well as nontarget sites. Future experimental studies should address whether CMV reactivation exacerbates SARS-CoV-2 pathogenesis.



ADDITIONAL KEY INFORMATION

UC DAVIS CALIFORNIA NATIONAL PRIMATE RESEARCH CENTER

UC DAVIS GRADUATE GROUP IN IMMUNOLOGY

UCSF Experimental Medicine Department of Medicine

CENTER FOR IMMUNOLOGY & INFECTIOUS DISEASES