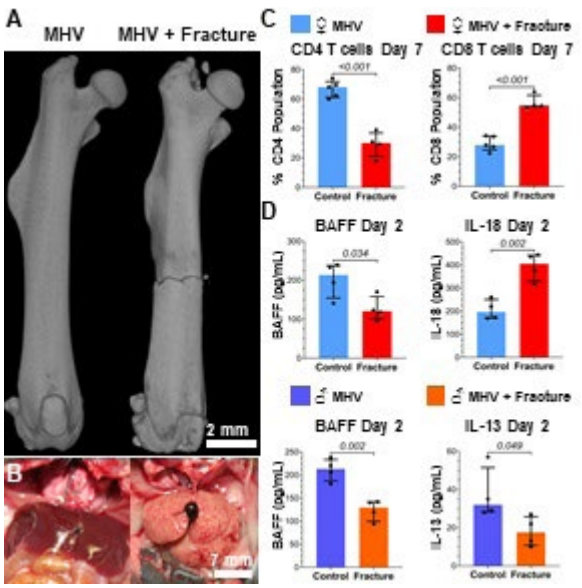
Influence of Murine Hepatitis Virus on Systemic Inflammatory Response After Femur Fracture

Ramkumar Tiruvannamalai Annamalai, PhD; Matthew Patrick, BS;
***Jeffrey A. Foster, MD**; Arun Aneja, MD, PhD*

Purpose: COVID-19, caused by SARS-CoV-2, has evolved into an international public health emergency and pandemic. There has been concern that the additional hit of orthopaedic injury, particularly long bone fracture, exacerbates the primed hyperinflammatory state of COVID infection. Murine coronavirus (MHV) shares a common genus with SARS-CoV-2 and presents with similar inflammatory symptoms. It provides an opportunity to study the comorbidities of COVID without substantial risk to the researchers. The objective of this study was to gain insight into how COVID infection and fracture impact the systemic immune response in male and female mice.

Methods: Four groups (n = 5) of C57BL/6 mice (Male MHV, Male MHV+Fracture, Female MHV, and Female MHV+Fracture) were examined. Two days prior to fracture, the infected groups were inoculated with MHV-A59 at 104 PFU intranasally. Fractures were created according to a previously established murine transverse fracture model, 32A3, and stabilized using a 15.2-mm titanium nail. Peripheral blood was collected before infection as a baseline and at 2 and 7 days post-fracture. Blood was separated into cells and plasma and analyzed through flow cytometry and a 48-analyte inflammatory multiplex assay, respectively.

Results: Mice femurs were successfully fractured 2 days post MHV infection (Fig. 1A). All control, MHV, mice had healthy livers, while some in the MHV+Fracture groups had visible liver damage in both sexes (Fig. 1B). Seven days post-fracture the CD4 T-cell population in the female MHV+Fracture was greatly reduced while the CD8 T-cell population was considerably increased (Fig. 1C). Both sexes fractured groups had a large decrease in B-cell activating factor (BAFF) (Fig. 1D), while the fractured female group alone had an increase in interleukin (IL)-18 and male fracture group alone had a decrease in IL-13. Interestingly, 1 male and 1 female mouse in the fractured group died before reaching the 7-days post-fracture end point.



Conclusion: MHV-infected male and female mice with fractures had an altered immune response. This study implies that fracture, while infected with a similar virus, like COVID-19, could influence the virus effect on the body.