SARS-CoV-2 Variants of Concern in Syrian Golden Hamsters

Kelsey Burenheide; Knight, Brittany; Bradrick, Shelton; Solocinski, Kristin; Miller, Joy; Michelotti, Julia; and Popescu, Luca

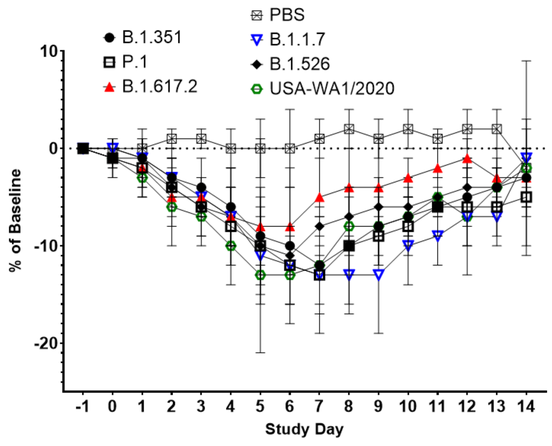
Introduction

SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) is the causative agent for the COVID-19 global pandemic, affecting countries all over the world. COVID-19 causes upper respiratory illness in humans ranging from mild symptoms like coughing or fever to severe symptoms like pneumonia and death. SARS-CoV-2 infects human cells by binding to the ACE2 receptor. Syrian golden hamsters express an ACE2 protein similar to humans making them a good animal model for SARS-CoV-2. We infected Syrian golden hamsters with different variants of concern of SARS-CoV-2 by intranasal instillation. We measured body weight loss, viral titers in serum, lungs, trachea, and nasal turbinates, development of neutralizing antibody response. Our results demonstrated that SARS-CoV-2 behave similarly in the hamster, thus confirming that it is a robust animal model for evaluation of new medical countermeasures.

Methods

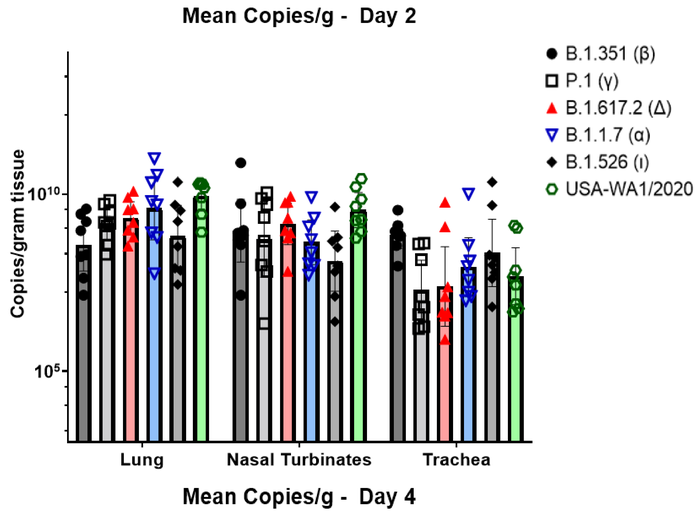
Syrian golden hamsters, half male and half female, ranging from 15-20 weeks of age were randomized by weight into groups of 8 animals per variant per sacrifice time point. Hamsters were exposed with one of the following SARS-CoV-2 variants: B.1.617.2 (delta), B.1.1.7 (alpha), B.1.526 (iota), B.1.351 (beta), P.1 (gamma), or USA-WA1/2020. Phosphate-buffered saline (PBS) was used for the group of control animals. All hamsters were exposed by intranasal (IN) route on Study Day 0 under isoflurane sedation. Animals were observed twice daily for clinical symptoms, respiration rate, and respiration quality score. Body weights were measured daily for all animals. Serial sacrifices were done on Study Day 2, 4, 7, or 14; blood was collected terminally via caudal vena cava or cardiac route. Lungs, trachea, and nasal turbinates were collected for all animals at the time of necropsy. Tissues were homogenized and RT-qPCR assay was performed to quantify viral RNA present in the tissues. A neutralization assay (MN) was performed to quantify neutralizing antibodies in sera collected. Lungs and trachea were sent off for histopathology.

Body Weight Loss



- Significant body weight loss versus control groups from 2 to 13 days post-infection (DPI) for all variants
- Maximum weight loss at 6-7 DPI for all variants
- Weights begin to rebound in all groups given SARS-CoV-2 after 7 DPI

Viral Burden



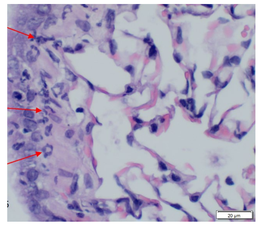
- Viral levels in tissues peaked on 2 DPI and 4 DPI
- There is a slight decrease from 2 to 4 DPI in lungs, nasal turbinates, and trachea.

Contact Information

Kelsey Burenheide
T: (816) 326-5050
E: kburenheide@mriglobal.og

MRIGlobal – KC HQ
425 Dr. Martin Luther King Jr. Blvd.
Kansas City, MO 64110

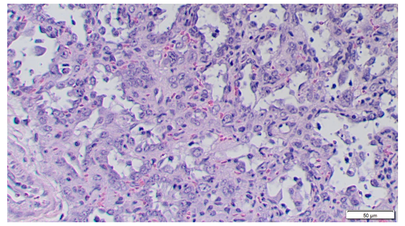
Lung Pathology



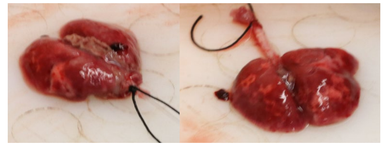
4 DPI

4 DPI lung
- Histopathology shows bronchiolitis
- Gross pathology shows multifocal areas of congestion and necrosis.

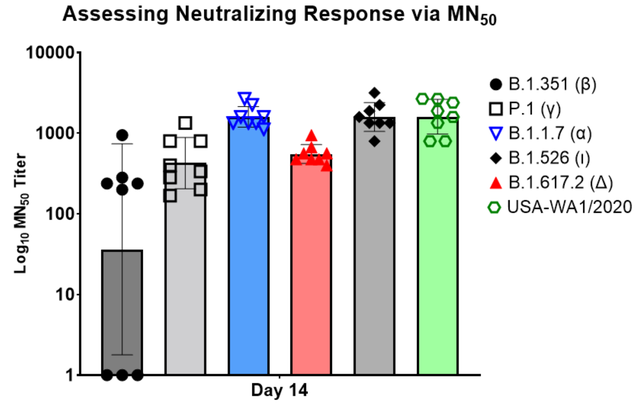
7 DPI lung
- Histopathology results show moderate increase in alveolar macrophages and mixed monocytes
- Gross pathology shows severe interstitial thickening (inflammation) showing alveolar walls greatly thickened by influx of inflammatory cells and hyperplasia



7 DPI



Antibody Response



Conclusions

- Hamster Model of SARS-CoV-2 shows consistency across the isolates used in infection studies: USA-WA1/2020 reference or Variants of Concern
- Minor pathogenic differences between isolates may exist but do not alter endpoints that are appropriate for MCM evaluation in the model
- Weight loss, organ histopathology (lung weight surrogate), viral load, and serum neutralization collected at time points presented are consistent with previous natural history studies using WA1