SARS-CoV-2 Omicron-B.1.1.529 Variant leads to less severe disease than Pango B and Delta variants strains in a mouse model of severe COVID-19.
Experimental Design

K8-hACE2 transgenic mice, male and female, 6-8 weeks old, Charles River

- **Lineage B** (LIV) UK strain of SARS-CoV-2 (hCoV-19/England/Liverpool_REMRQ0001/2020)
- **Delta; B.1.617.2;** hCoV-19/England/SHEF-10E8F3B/2021 (GISAID accession number EPI_ISL_1731019)
- **Omicron; B.1.1.529;** M21021166 isolated in Oxford, England. Contains A701V
- All virus stocks deep sequenced to confirm identity and lack of additional changes.

Use K18-hACE2 Tg mice: Infect i.n. with SARS-CoV-2 Strains Pango B, Delta or Omicron @10³ PFU

**Day 0**
- Lungs
- Nasal tissue

**Day 2**
- RT-qPCR
- Pathology

**Day 4**
- Throat swabs taken

**Day 6**
- qPCR
K18-hACE2 mice infected with Omicron lose weight but recover.
Omicron variant-infected mice have lower viral loads

- Mice infected with Omicron virus have approx. 2 log less viral load in swabs (d2), nasal tissue and lung tissue (d6)
Histopathology, lung (6 dpi)

Pathological changes:
- Type and distribution identical
- Differing extent
  (Lineage B/Delta > Omicron)

Morphometric analysis:
Significantly less consolidation of lung parenchyma with Omicron infection
Histopathology, lung (6 dpi)

SARS-CoV-2 N expression:
- Target cells identical
- Quantitative differences

Morphometric analysis:
Significant differences in viral antigen expression:
Lineage B > Delta > Omicron
Histopathology, lung (6 dpi)

Type II pneumocytes:
- Activation
- Syncytial cell formation

Lineage B

Delta

Omicron

SARS-CoV-2 N
Histopathology, 6 dpi

Infection of the brain:
- Frequent with Lineage B (6/6) and Delta (3/6)
- Not observed with Omicron
**Omicron variant-infected mice have lower viral loads**

Day 1 lung viral titre

Day 1 post-infection. Lung. SARS-CoV-N

- Omicron variant-infected mice have lower viral loads compared to Delta.
Ronapreve (REGN-CoV) lacks efficacy against the SARS-CoV-2 Omicron variant

- Ronapreve (REGN-COV2), is composed of two monoclonal antibodies (casirivumab and imdevimab), has shown efficacy against previous variants of SARS-CoV-2
- In vitro neutralisation studies have demonstrated compromised activity of Ronapreve against Omicron variant
- Aim to investigate activity against Omicron in an animal model to provide an in vivo validation of prior in vitro assay readouts.

Use K18-hACE2 Tg mice: Infect i.n. with SARS-CoV-2, Delta or Omicron @10^3 PFU

Ronapreve 400μg or PBS IP

Day 0

Day 1

Day 4

Day 6

n = 6/group

Lungs

Nasal tissue

RT-qPCR
Ronapreve (REGN-CoV) lacks efficacy against the SARS-CoV-2 Omicron variant

Lung tissue d6

Day 4

Day 6
Conclusions

- Omicron variant causes weight loss but is associated with recovery unlike Pango B and Delta infected mice.
- Mice infected with Omicron have higher viral load at d1 post-infection but much lower after that.
- Omicron-infected mice also had severe pathological changes and virus antigen with no virus antigen in nasal tissues (d6) or brain.
- Ronovpreve monoclonal antibody therapy ineffective against the omicron variant.

Suggests that replication of Omicron variant occurs very early during infection but disease associated with the Omicron variant is less severe than with Pango B or Delta variant viruses.

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