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.

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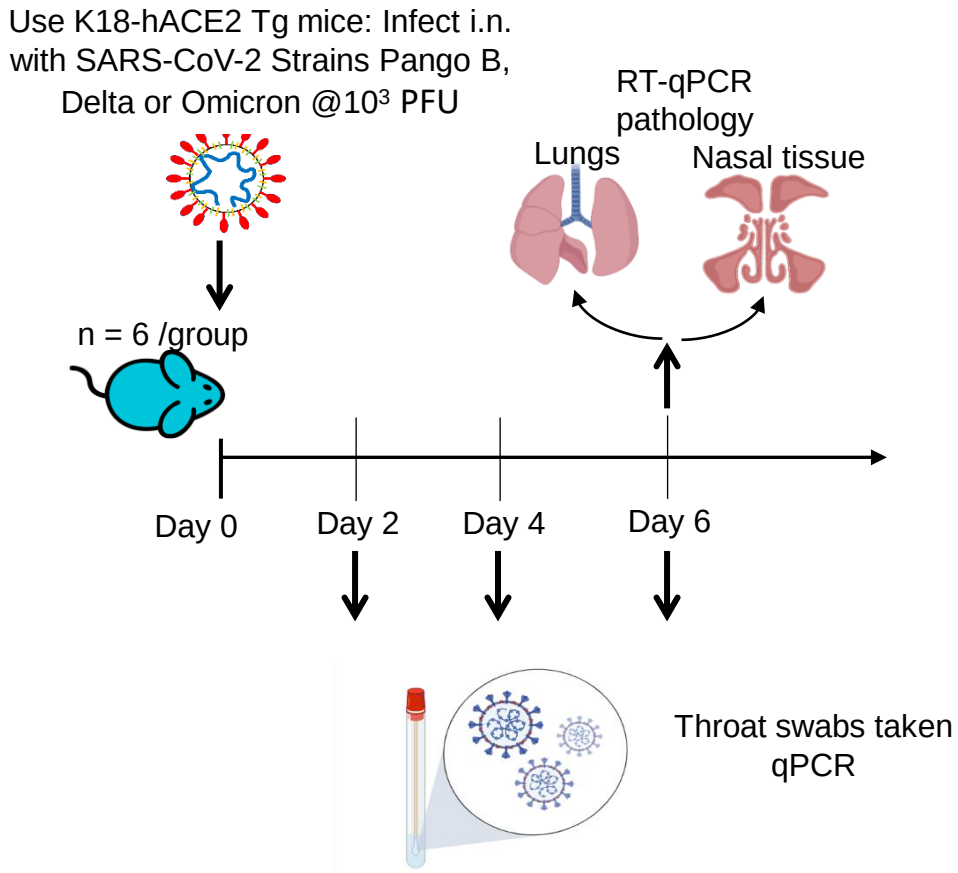
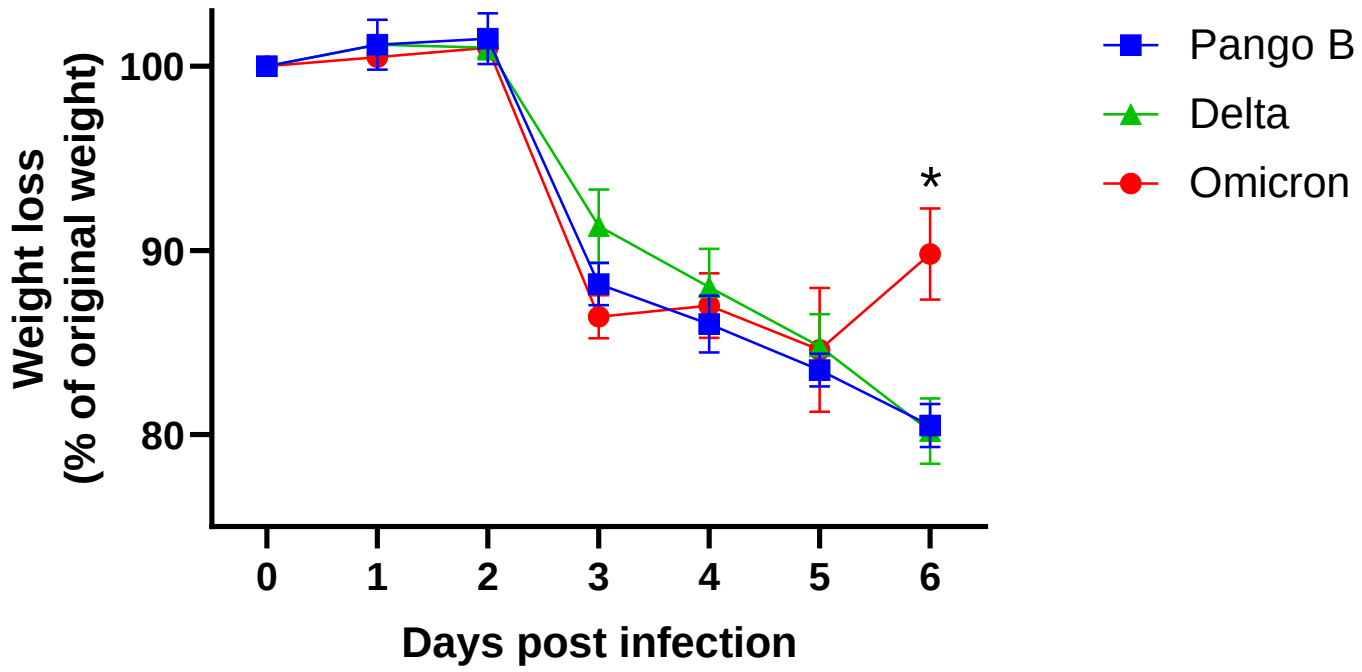
Experimental Design

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

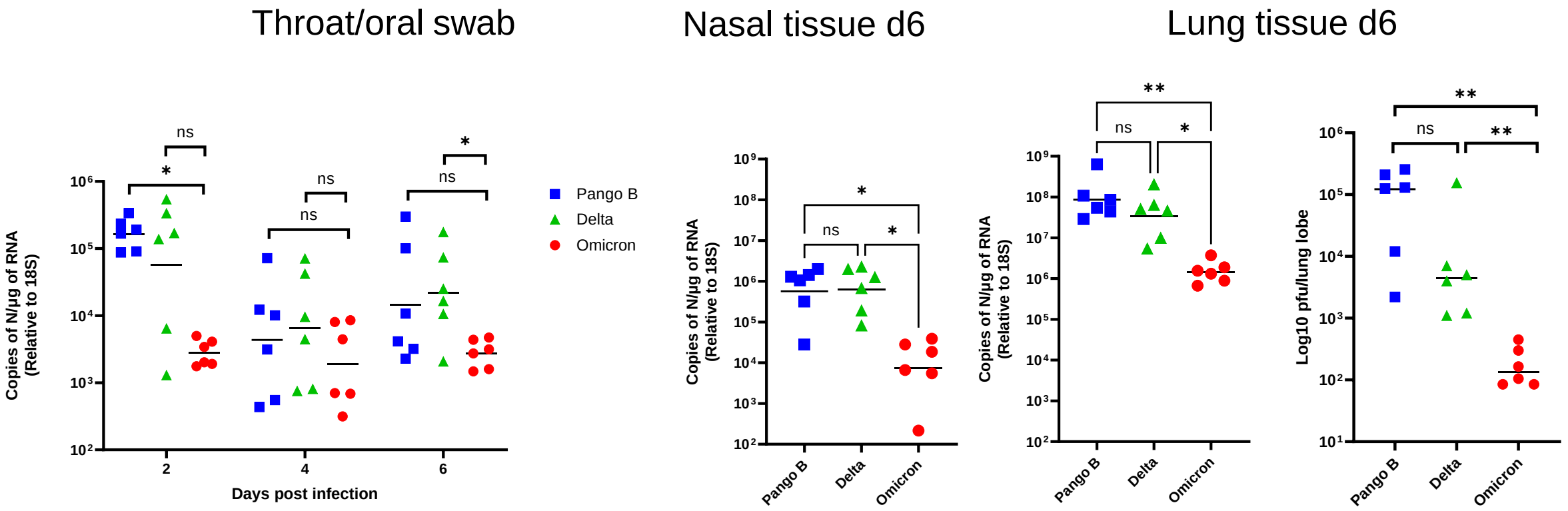
- **Lineage B** (LIV) UK strain of SARS-CoV-2 (hCoV-19/England/Liverpool_REMRQ0001/2020)
- **Delta; B.1.617.2;** hCoV-19/England/SHEF-10E8F3B/2021 (GISAID accession number EPI_ISL_1731019)
- **Omicron; B.1.1.529;** M21021166 isolated in Oxford, England. Contains A701V
- All virus stocks deep sequenced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



K18-hACE2 mice infected with Omicron lose weight but recover



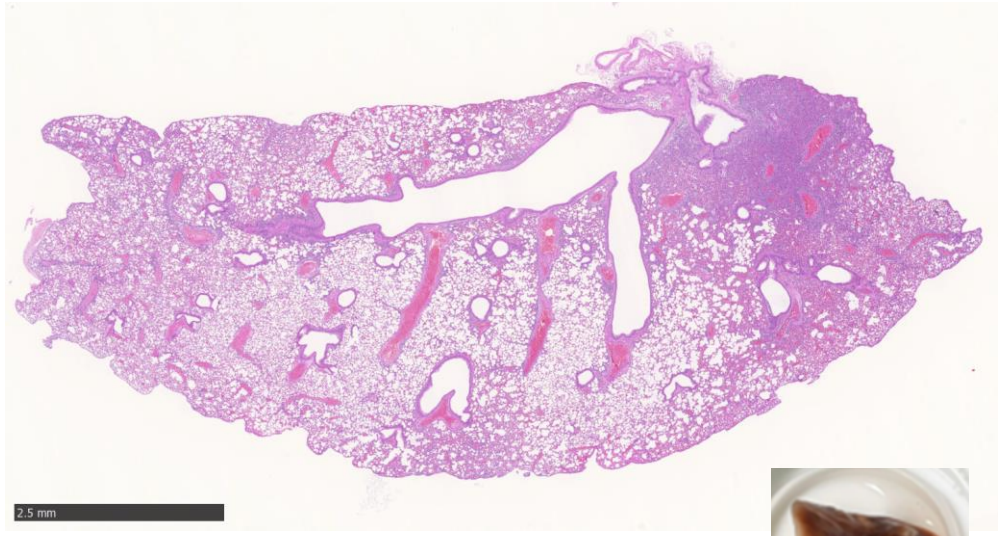
Omicron variant-infected mice have lower viral loads

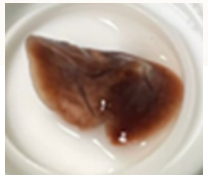


- Mice infected with Omicron virus have approx. 2 log less viral load in swabs (d2), nasal tissue and lung tissue (d6)

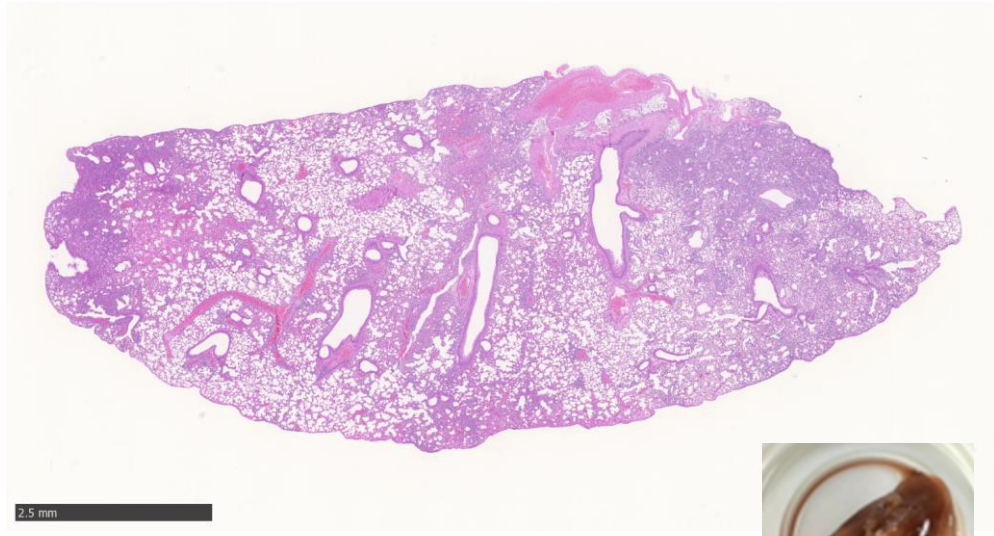
Histopathology, lung (6 dpi)

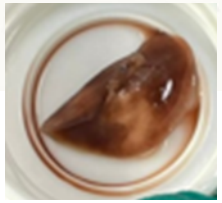
Pathological changes:
- Type and distribution identical
- Differing extent (Lineage B/Delta > Omicron)





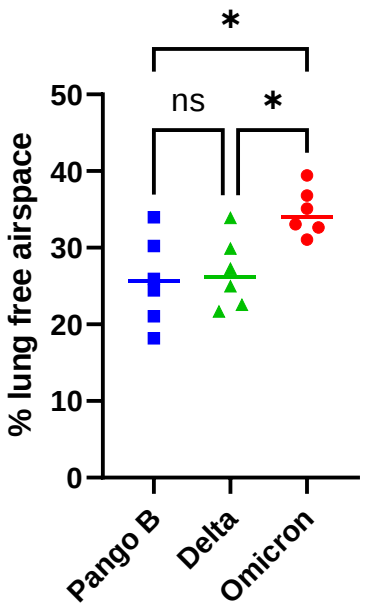
Lineage B





Delta

Morphometric analysis:
Significantly less consolidation of lung parenchyma with Omicron infection

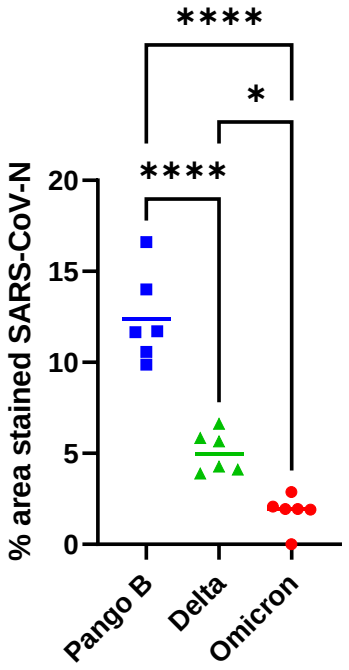


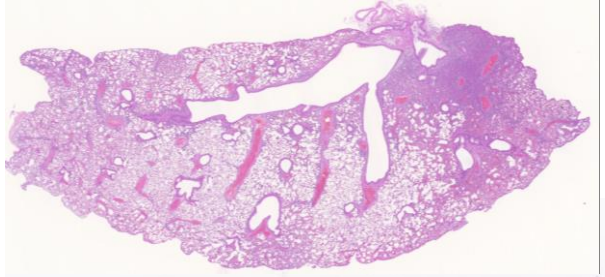
Omicron

Histopathology, lung (6 dpi)

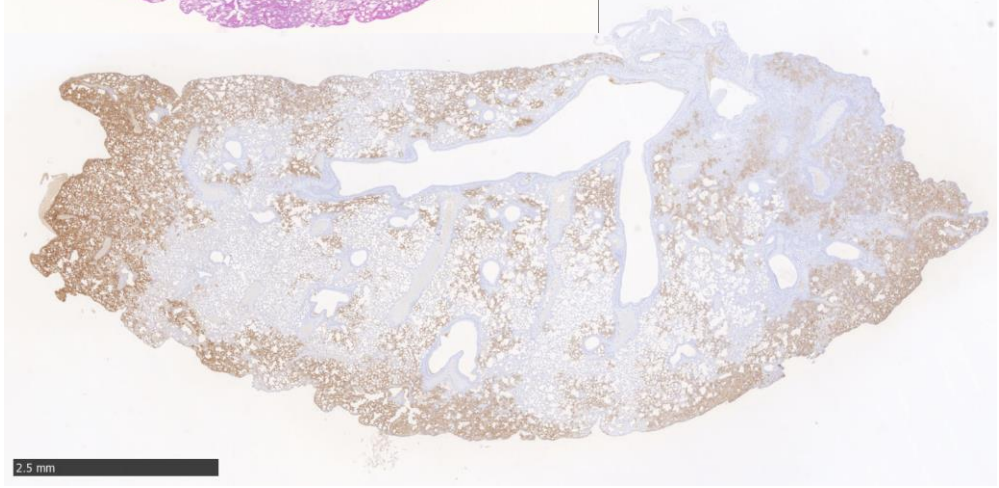
SARS-CoV-2 N expression:
- Target cells identical
- Quantitative differences

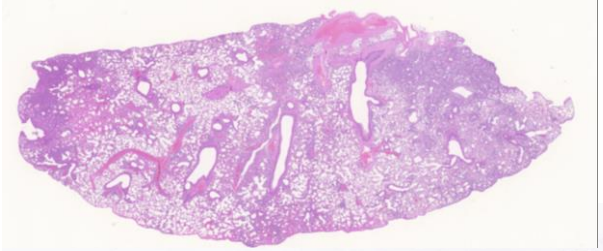
Morphometric analysis:
Significant differences in viral antigen expression:
Lineage B > Delta > Omicron



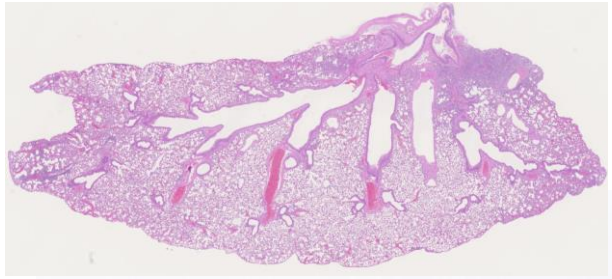


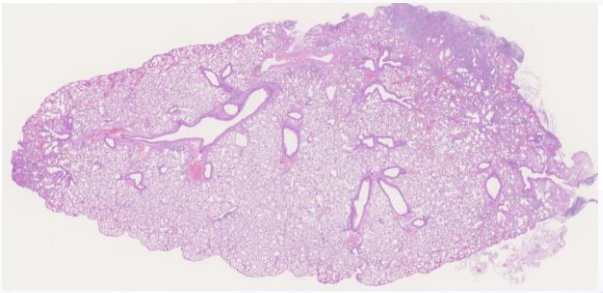
Lineage B



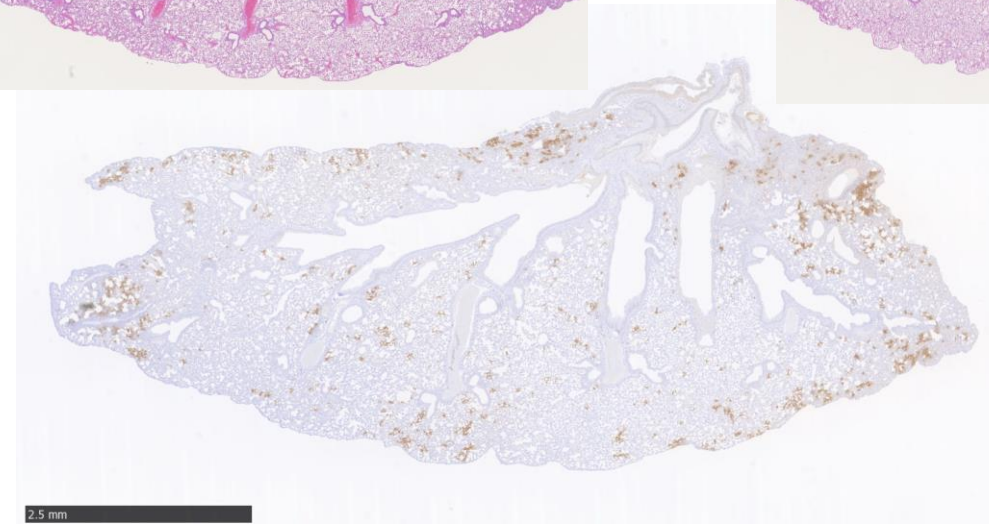


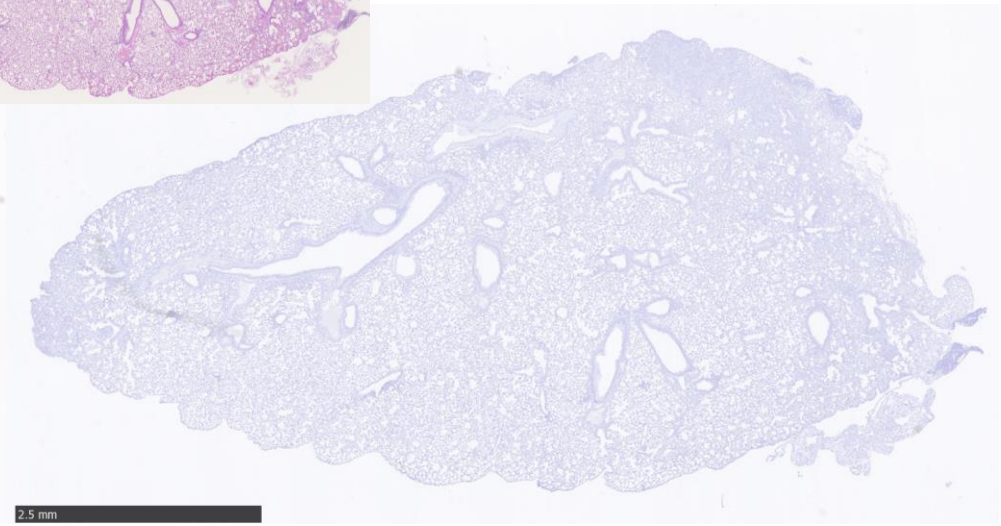
Delta





Omicron





Histopathology, lung (6 dpi)

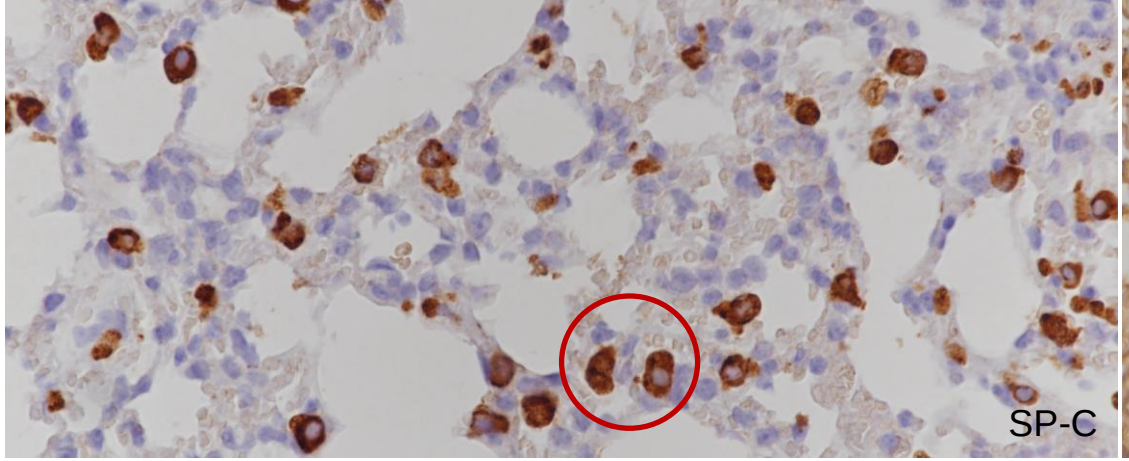
Lineage B

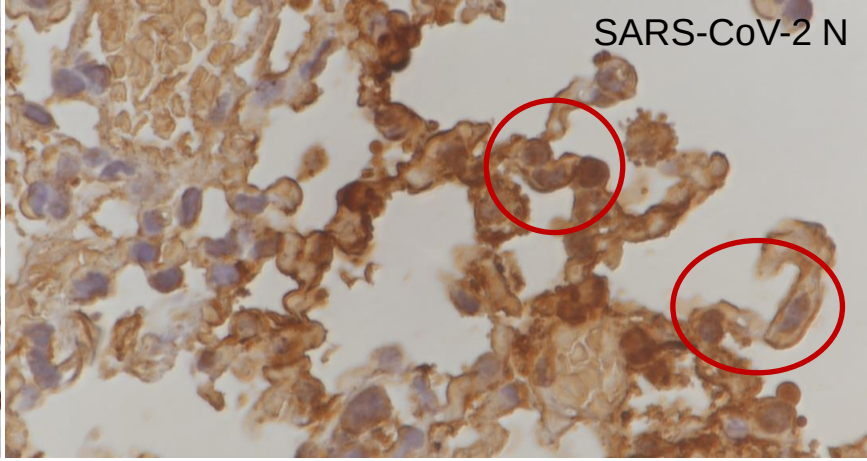
Delta

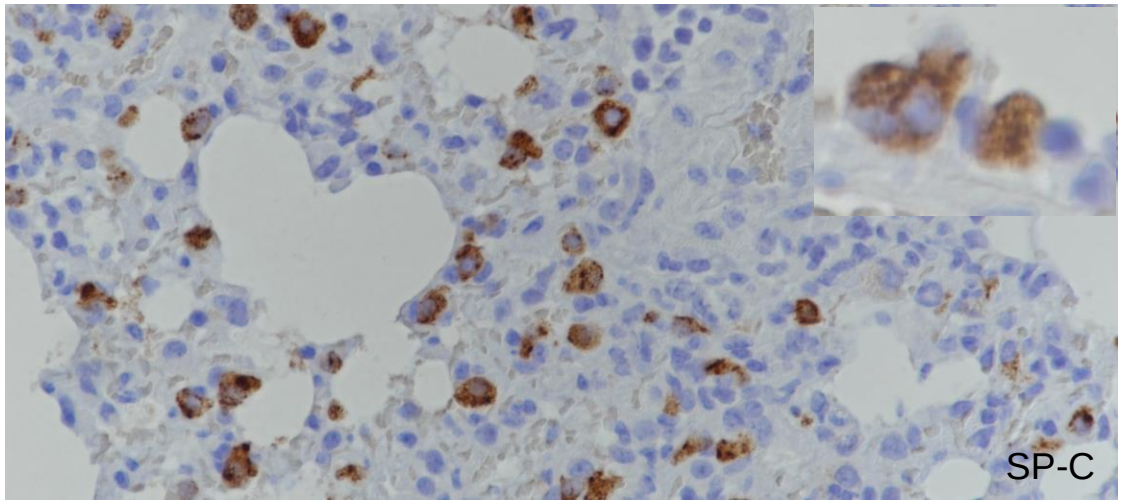
Omicron

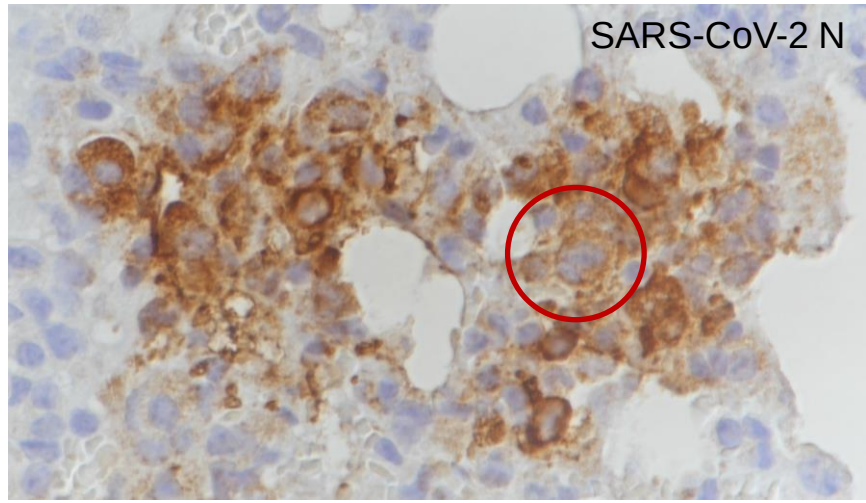
Type II pneumocytes:

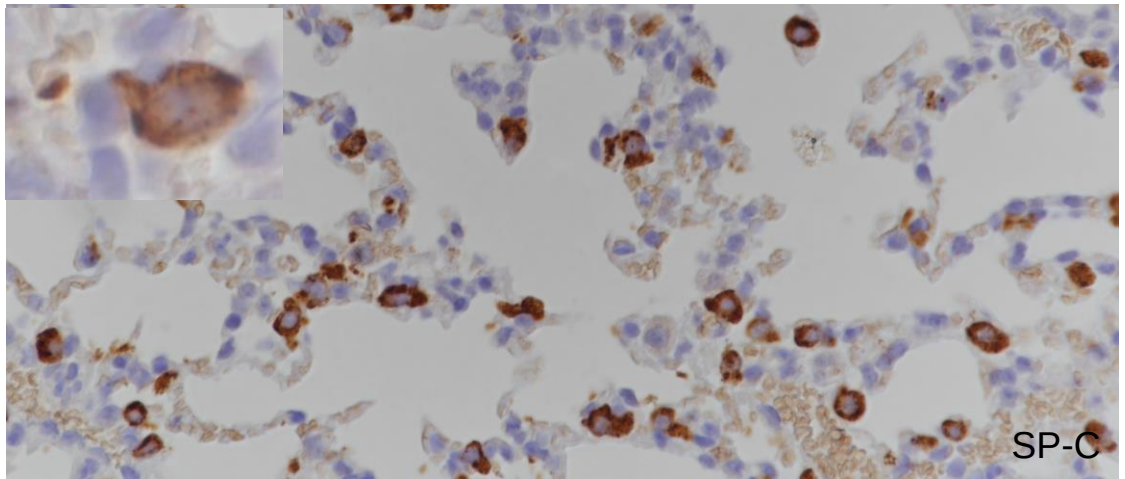
- Activation
- Syncytial cell formation

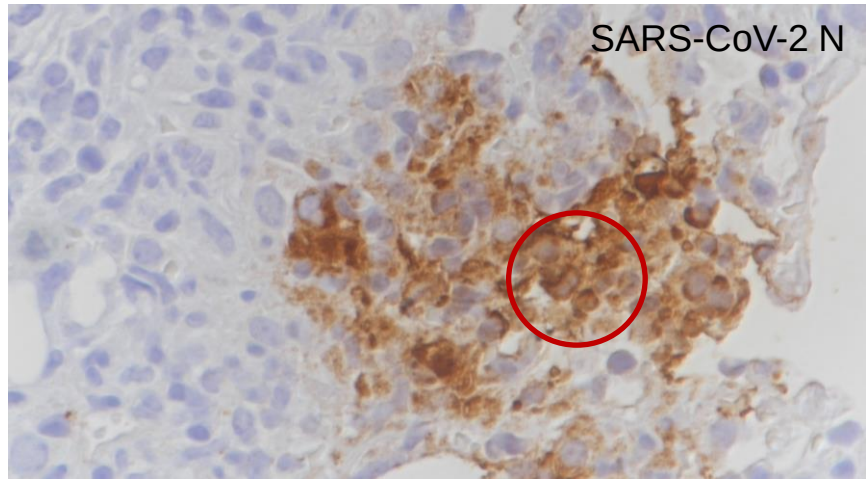








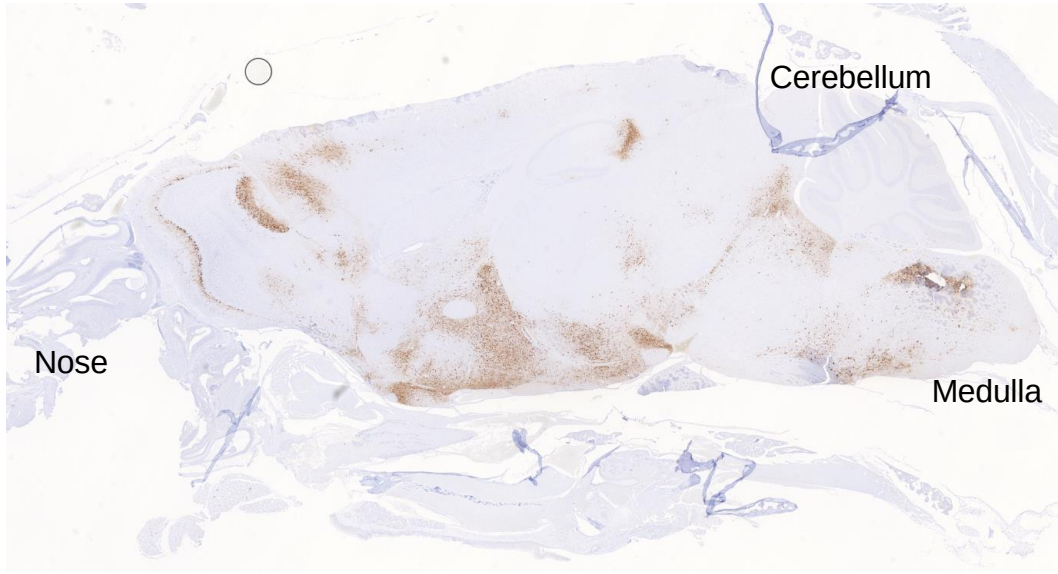




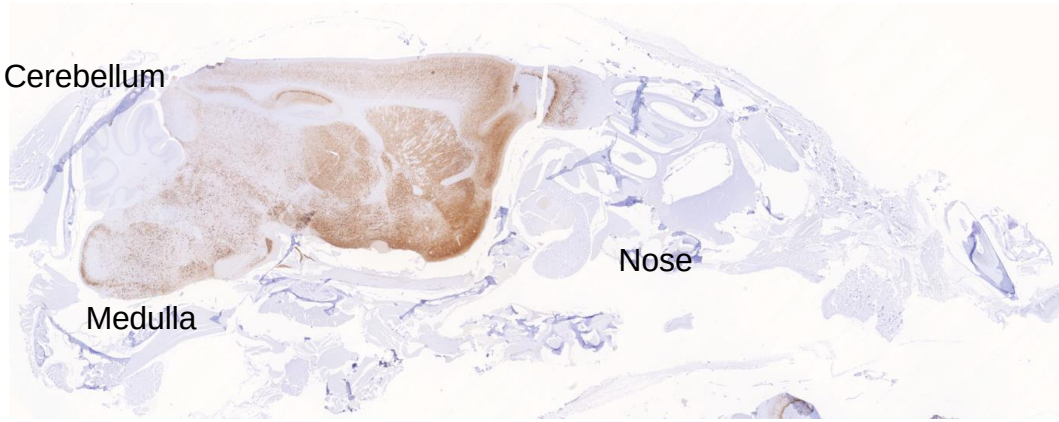
Histopathology, 6 dpi

Infection of the brain:

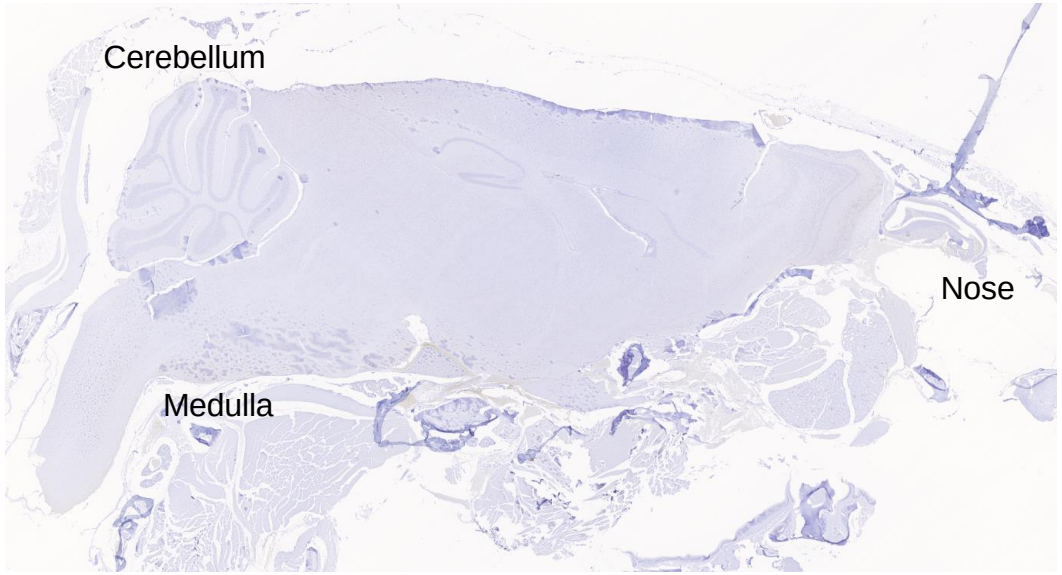
- Frequent with Lineage B (6/6) and Delta (3/6)
- Not observed with Omicron



Lineage B



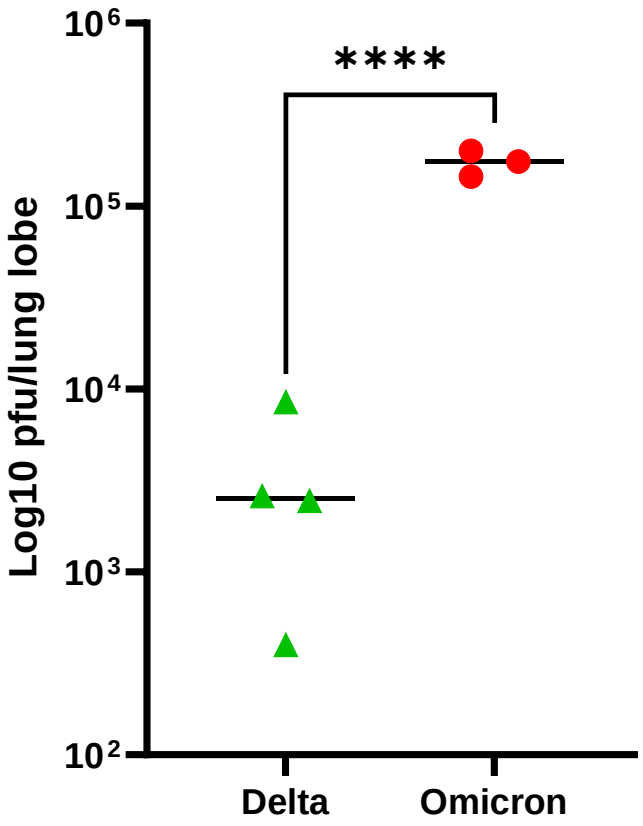
Delta



Omicron

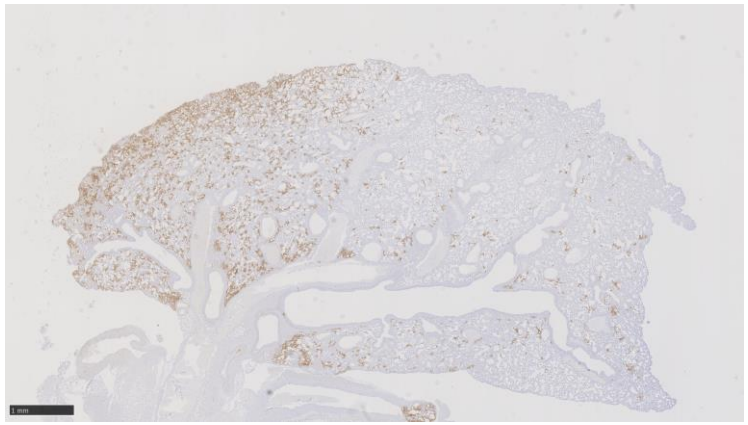
Omicron variant-infected mice have lower viral loads

Day 1 lung viral titre

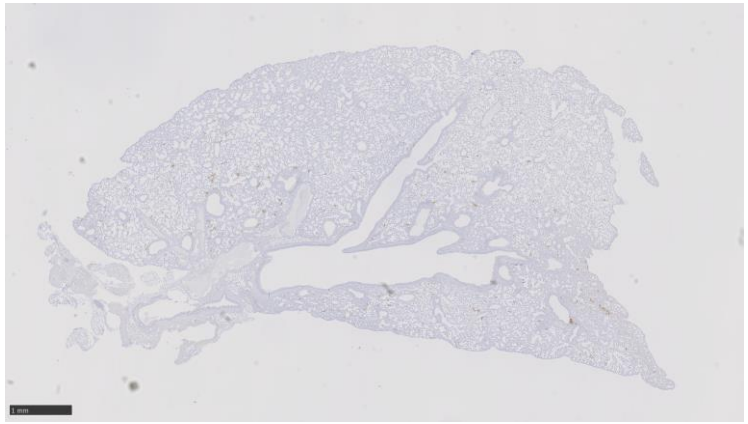


Day 1 post-infection. Lung. SARS-CoV-N

Omicron

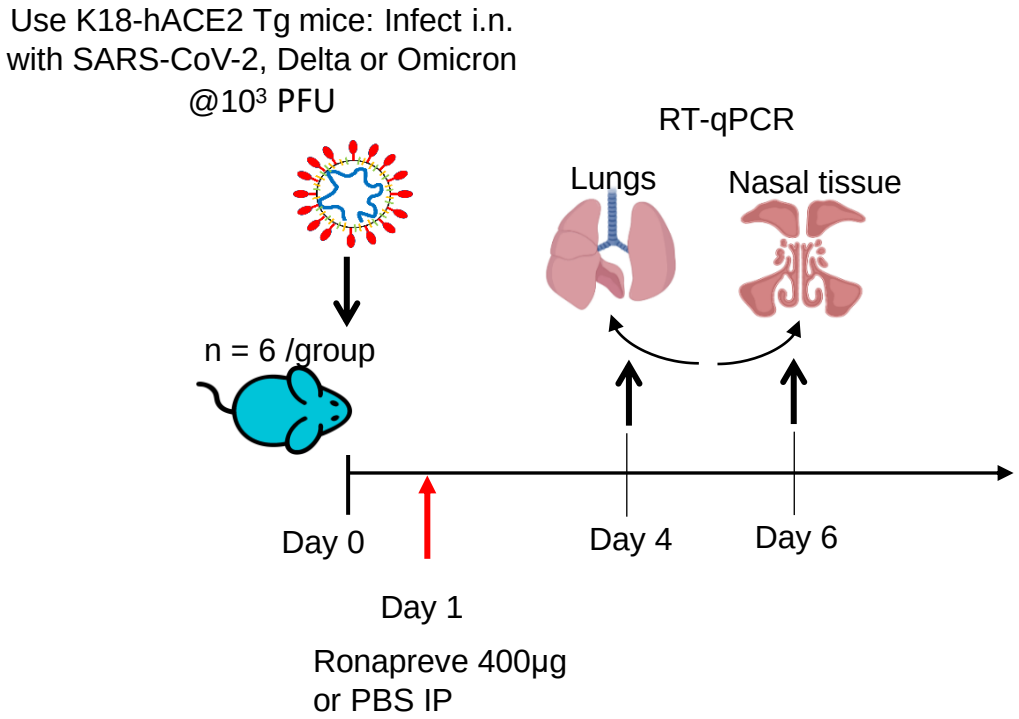


Delta



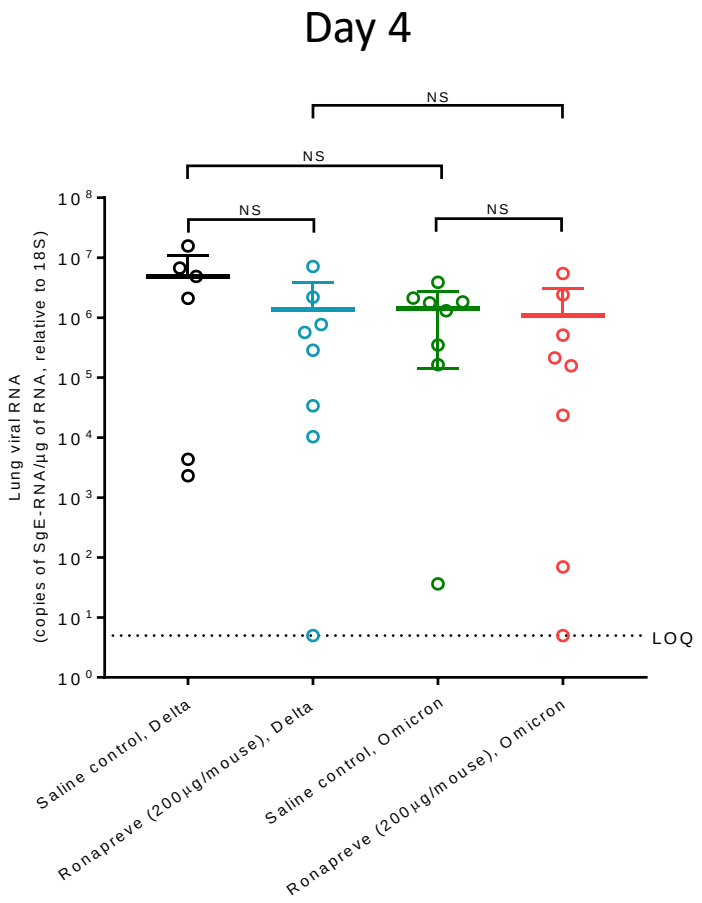
Ronapreve (REGN-CoV) lacks efficacy against the SARS-CoV-2 Omicron variant

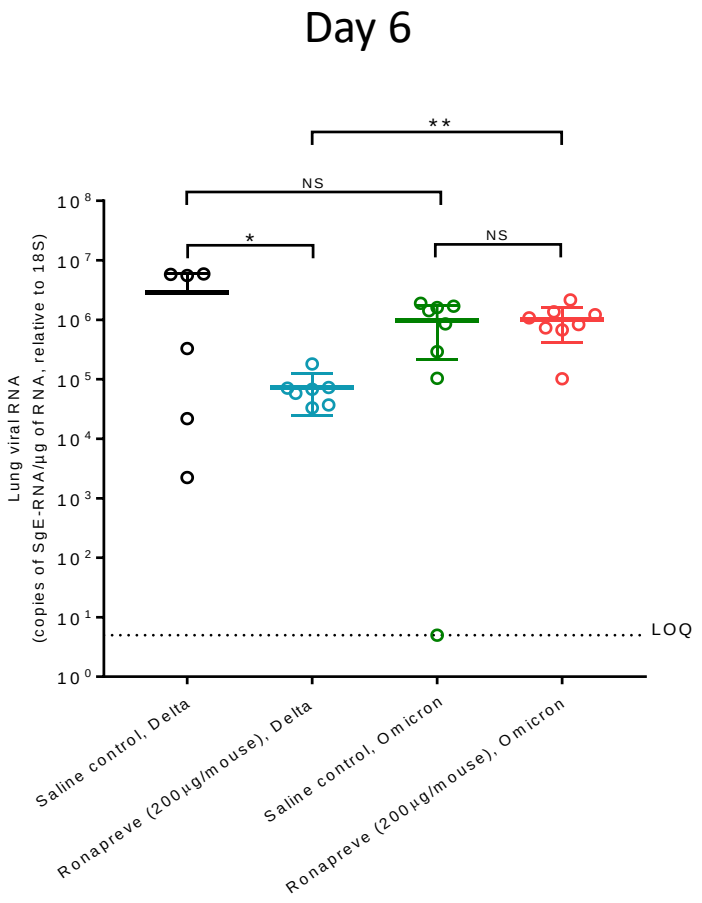
- Ronapreve (REGN-COV2), is composed of two monoclonal antibodies (casirivumab and imdevimab), has shown efficacy against previous variants of SARS-CoV-2
- In vitro neutralisation studies have demonstrated compromised activity of Ronapreve against Omicron variant
- Aim to investigate activity against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



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

Lung tissue d6





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.**

bioRxiv 2021.12.26.474085; doi: https://doi.org/10.1101/2021.12.26.474085
bioRxiv 2022.01.23.477397; doi: https://doi.org/10.1101/2022.01.23.477397

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