



UK Health
Security
Agency

Convalescence from prototype SARS-CoV-2 protects Syrian hamsters from disease caused by the Omicron variant

Pre-print:

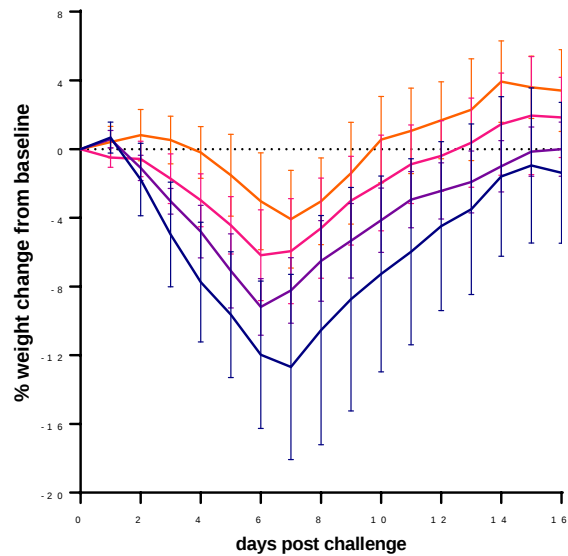
Ryan et. al. bioRxiv 2021.12.24.474081; doi: <https://doi.org/10.1101/2021.12.24.474081>

14th February 2022

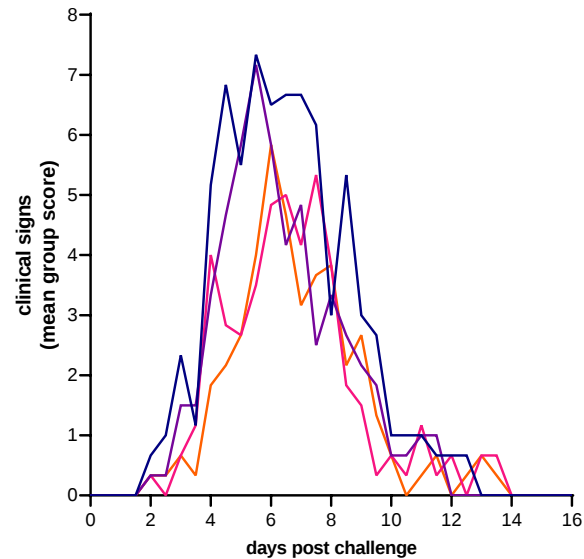
Dose-ranging Study initiated Oct 2021

Decreasing doses (PFU) of VIC01 produced a less severe disease in hamsters.
Viral shedding from URT (throat swabs) was similar regardless of dose given.

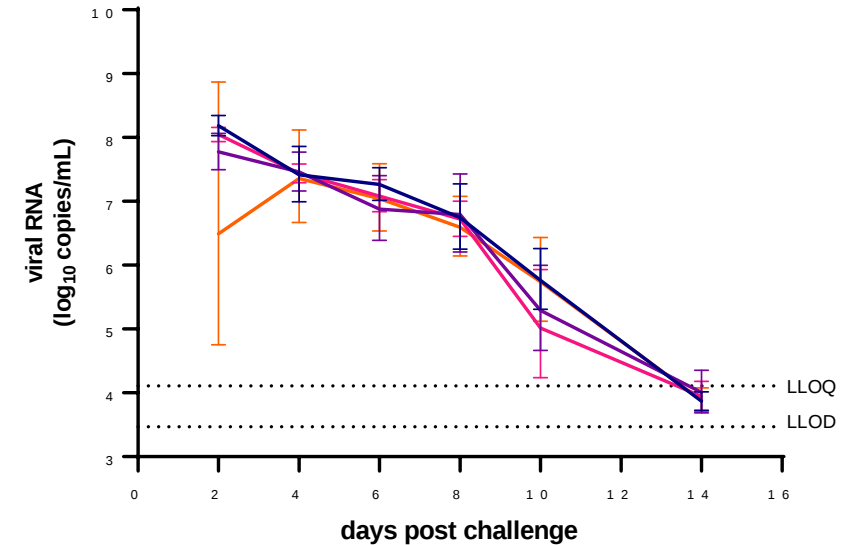
% weight change from baseline



Clinical Scores



Viral shedding from URT

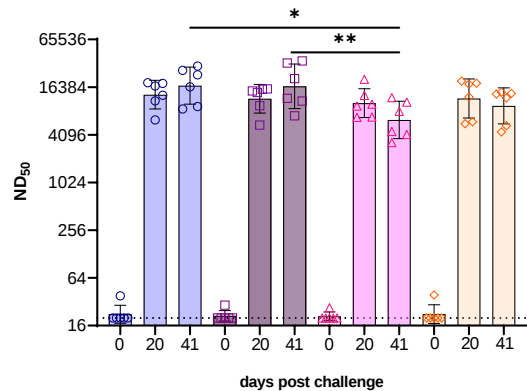


Clinical Sign	Score
Healthy	0
Lethargic	1
Eyes Shut	1
Behavioural Change	1
Sunken Eyes	2
Ruffled	2
Wasp Waisted	3
Coughing	3
Dehydrated	3
Hunched	3
Laboured Breathing (1) - occasional catch or skip in breathing rate	5
Laboured Breathing (2) - abdominal effort with breathing difficulties	7

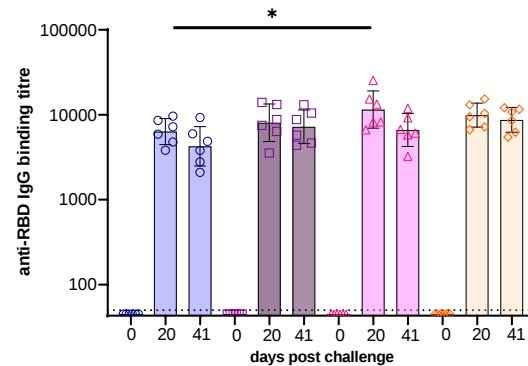
Assessment of Humoral Responses

The longitudinal humoral response to VIC01 was high & comparable irrespective of dose

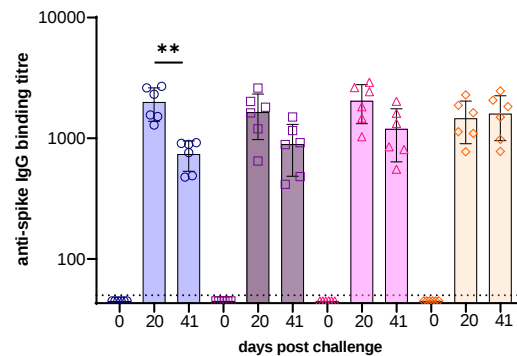
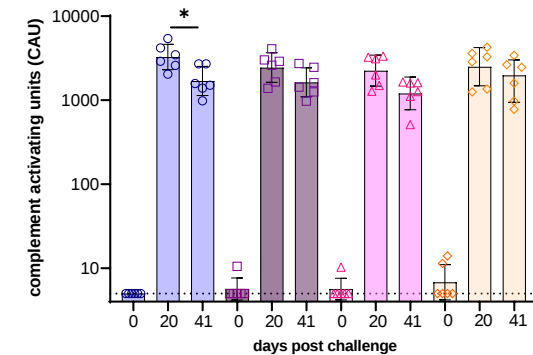
wt virus (VIC01) neutralisation



RBD & Spike IgG ELISA



Spike ADCC



- Omicron emerged ~ 30 DPC
- Opted to re-purpose the study for Omicron re-challenge

5E+04

5E+03

5E+02

1E+02

Hamster allocation for re-challenge

Re-challenge groups (n=12):

9328	M	Victoria
23369	F	
26638	F	

8694	M	Omicron
16480	M	
30243	F	

7121	M	Victoria
33027	M	
20956	F	

11813	F	Omicron
10913	M	
33027	F	

3271	F	Victoria
12056	F	
8081	M	

4124	M	Omicron
4528	M	
10589	F	

4456	M	Victoria
11947	M	
14052	F	

5322	M	Omicron
13410	F	
13657	F	

VIC01 5E+04

VIC01 5E+03

VIC01 5E+02

VIC01 1E+02

*day 41 ND₅₀ titres, re-challenged at day 50

Single challenge groups (age matched):

M	Victoria
M	
M	
F	
F	

M	Omicron
M	
M	
F	
F	

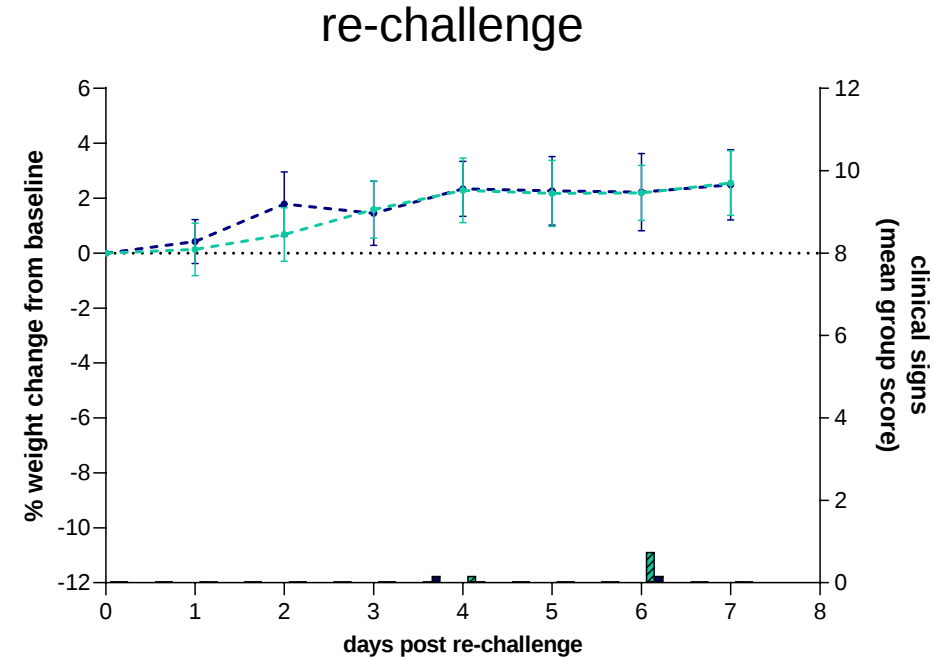
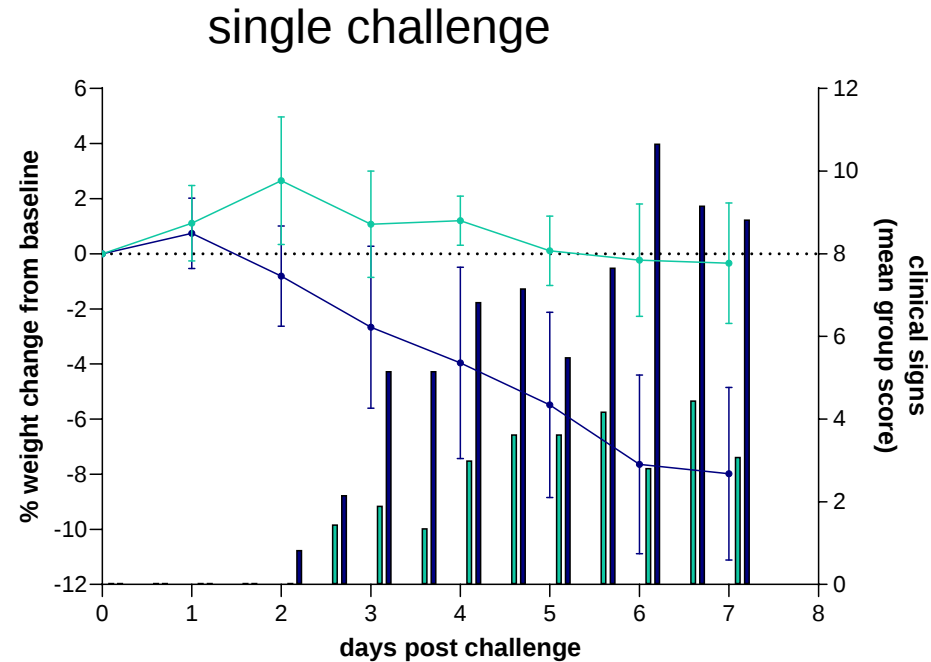
Challenge Virus:

VIC01 = 3.10E+03 FFU (target dose 5E+04 PFU)

Omicron = 8.18+03 FFU

Clinical Observations (culls at 7 DPC)

Omicron appeared to produced a milder disease in hamsters and all re-challenged hamsters appeared to be protected.



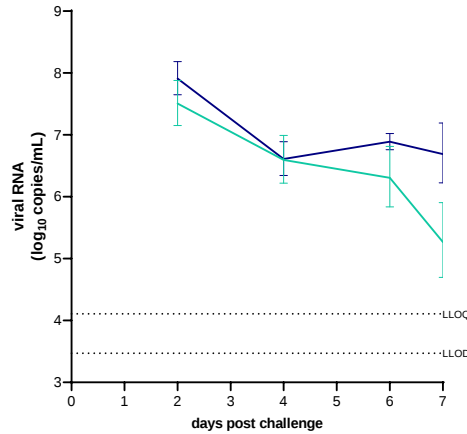
— VIC01 — Omicron

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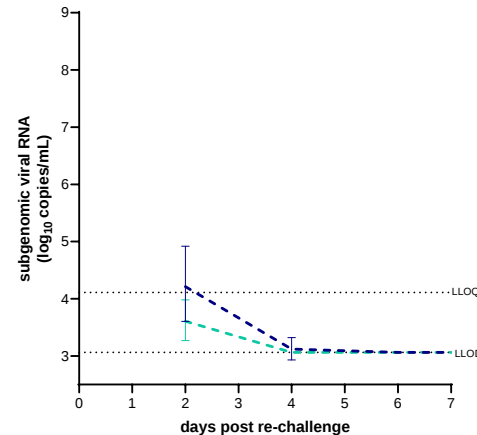
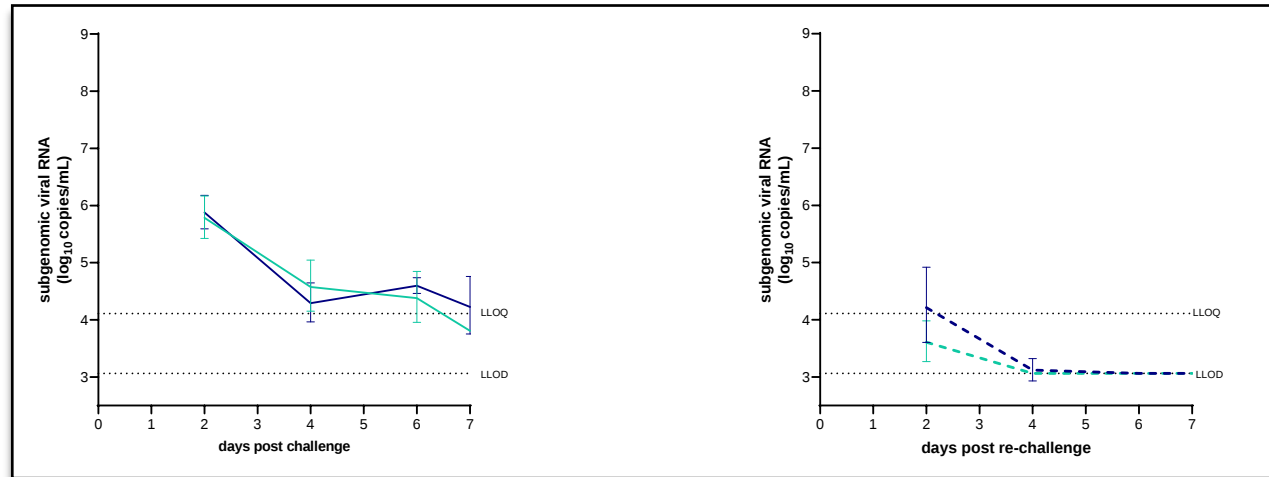
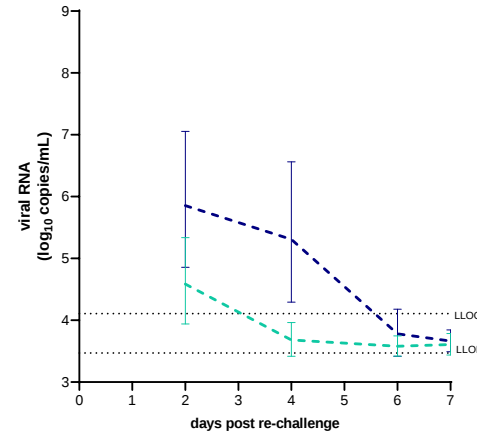
Viral Shedding (RT-qPCR)

Re-challenged hamsters experienced rapid clearance of virus from the URT (throat swabs)

single challenge



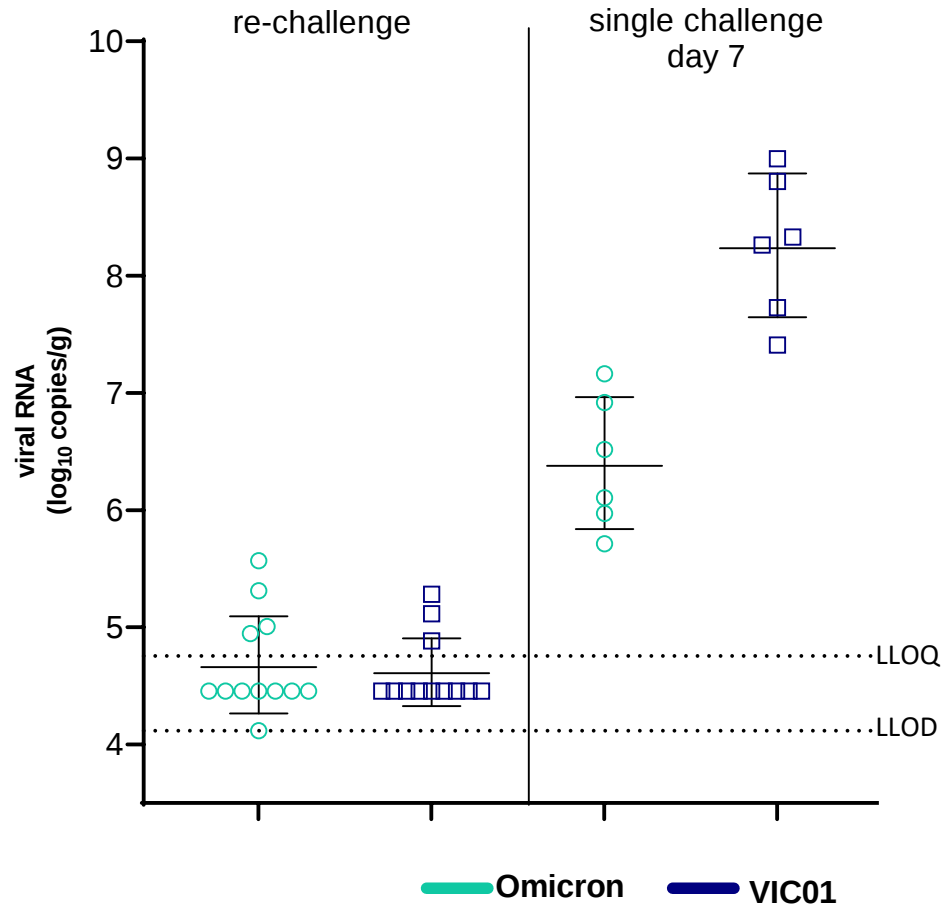
re-challenge



— VIC01 — Omicron

Viral Load in the Lungs (RT-qPCR)

The viral load in rechallenged hamsters shows protection against both VIC01 and Omicron compared to single challenge hamsters.



CDC N-gene PCR

Single challenge (7 dpc)

Significantly (P 0.0003) lower viral load in Omicron challenge hamsters compared to VIC01 challenges hamsters

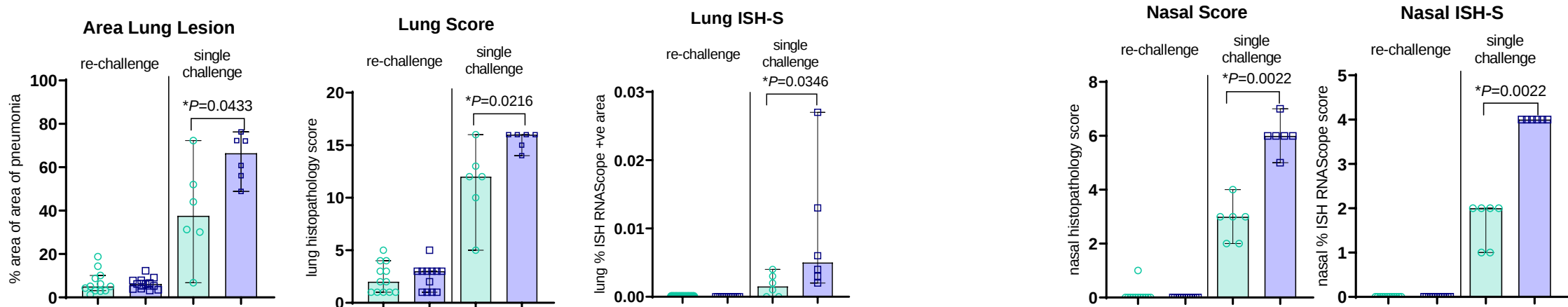
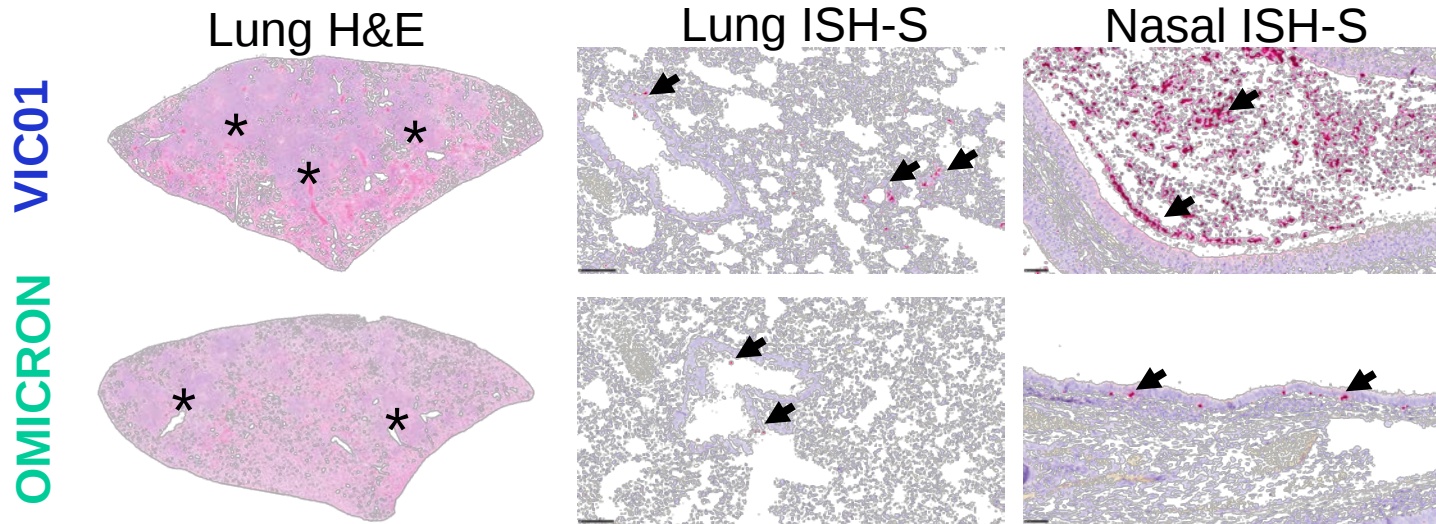
Rechallenge

No significant difference between VIC01 and Omicron rechallenge groups

Histopathology - Lung and Nasal Cavity

At day 7, viral load in the lungs of Omicron challenged hamsters was significantly lower.

Pathology in the lungs and nasal cavity was found to be milder omicron challenged hamsters.



Summary

- Omicron challenge resulted in less severe, but measurable disease
- Convalescence from VIC01 protected against Omicron challenge
- Hamster model has been valuable in COVID-19 vaccine, therapeutic and passive transfer studies.
- Evaluation of countermeasures against Omicron possible
 - Same endpoints; weight change, clinical signs, viral loads, lung/URT pathology
 - Less discriminatory power

Thanks

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Virus isolation, propagation & characterisation

In vivo team

Sample processing

Molecular virology

Pathology

Immunology

CEPI

Agility
Program

https://epi.tghn.org/covax-overview/enabling-sciences/agility_epi/