Infection and cross-protection with Omicron in K18-hACE2 mice

Kanta Subbarao, Mariana Baz, Danielle Anderson

WHO Collaborating Centre for Reference and Research on Influenza
Department of Microbiology and Immunology, University of Melbourne,
Peter Doherty Institute for Infection and Immunity

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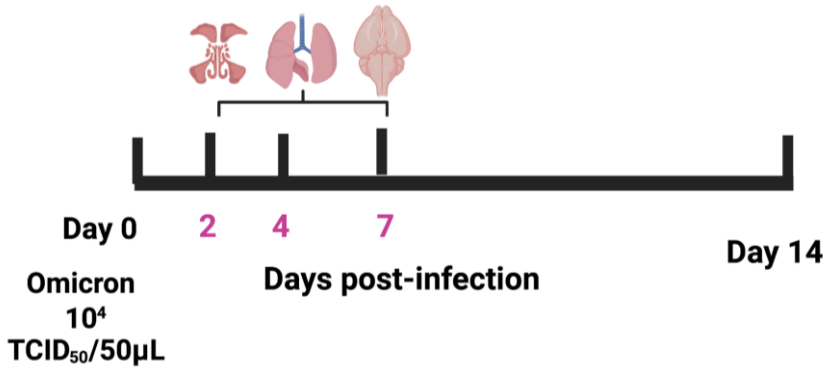
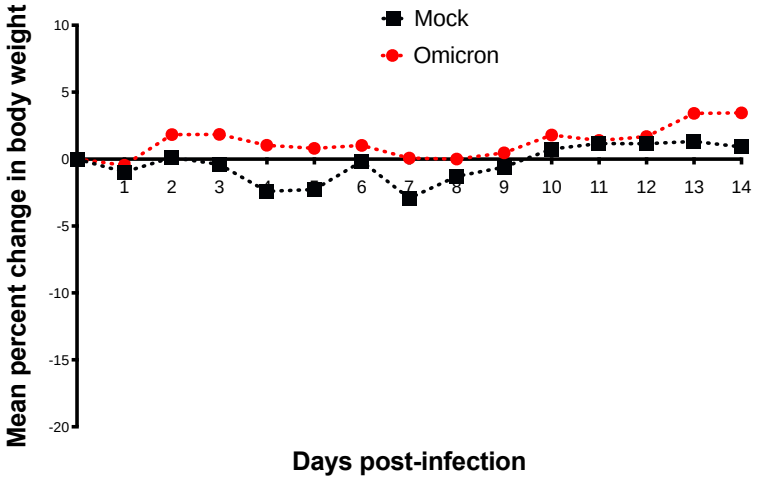
Doherty Institute
A joint venture between the University of Melbourne and the Royal Melbourne Hospital

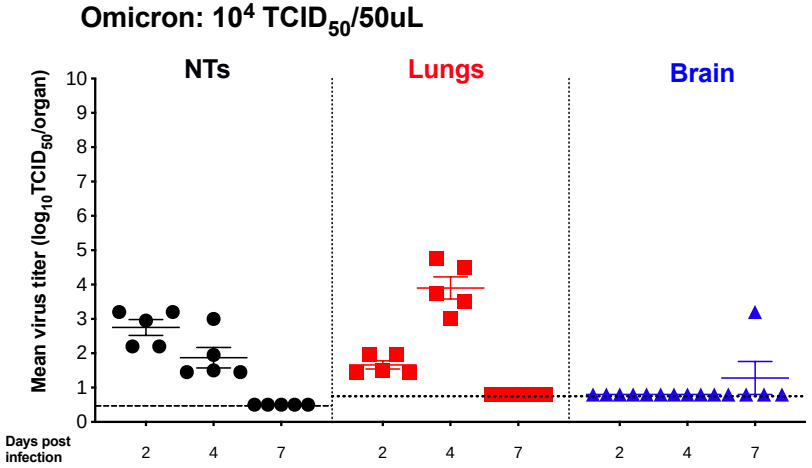
Objectives

- To determine the kinetics of replication of the Omicron variant in K18-hACE2 mice
- To determine whether primary infection with a low dose of Omicron virus protects from re-infection
- To determine whether primary infection with the Wuhan and Delta viruses protect against challenge with Omicron
- To determine cross-neutralizing Ab responses following primary infection with the Wuhan and Delta viruses

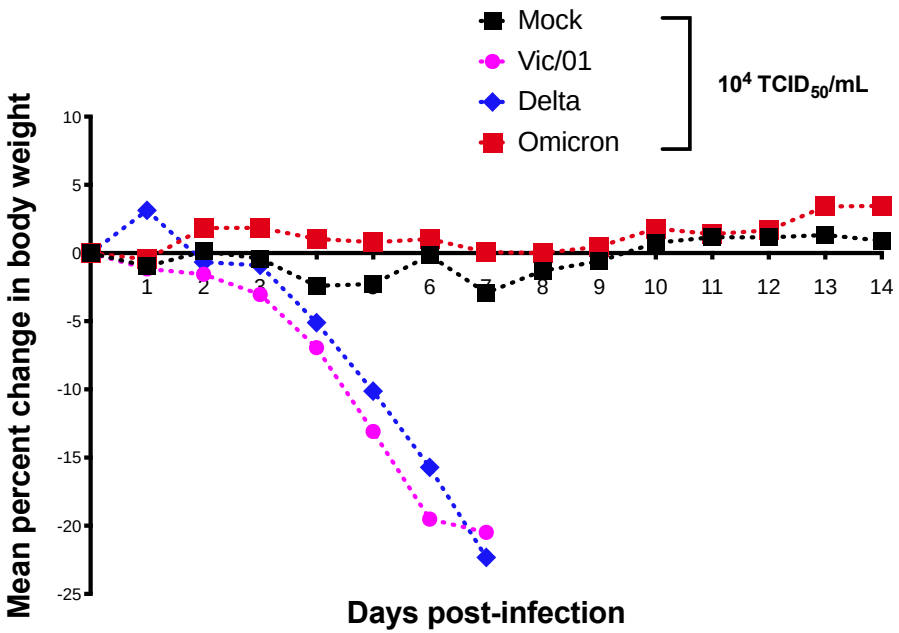
Infection of K18-hACE2 mice with the Omicron variant

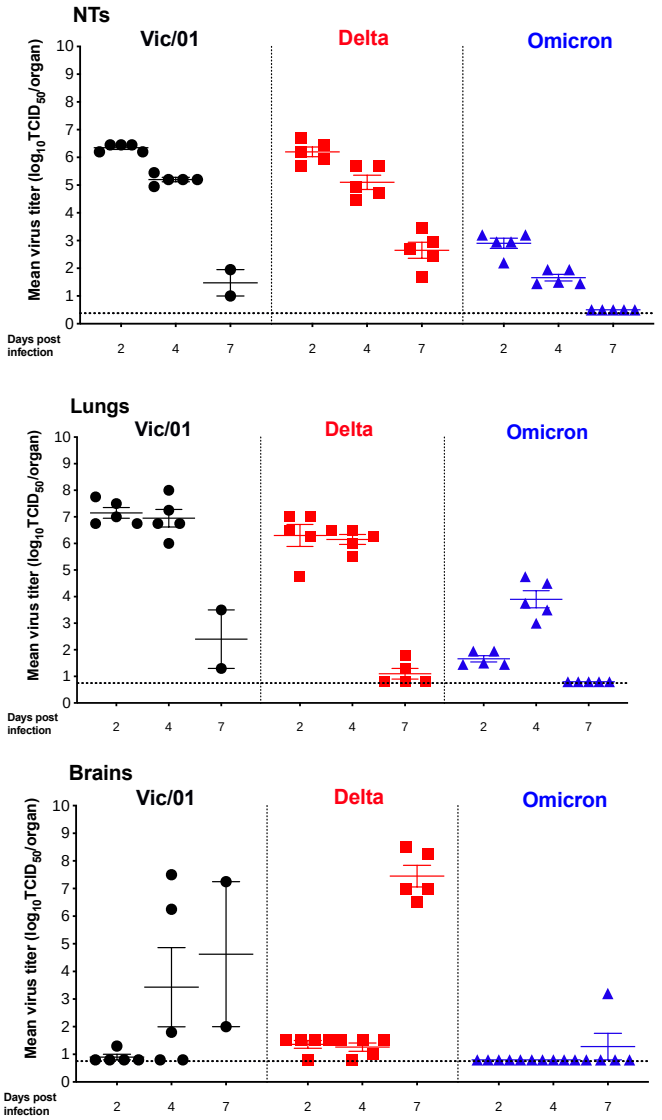






Comparison with Ancestral and Delta strains

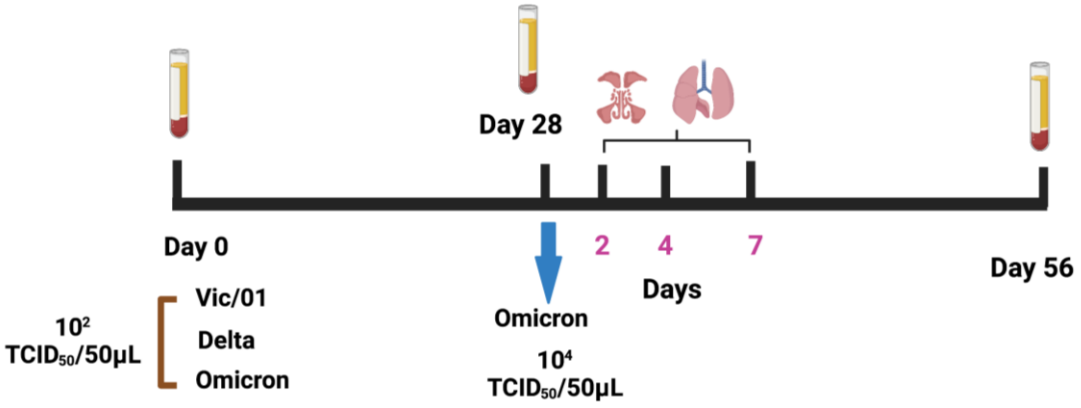


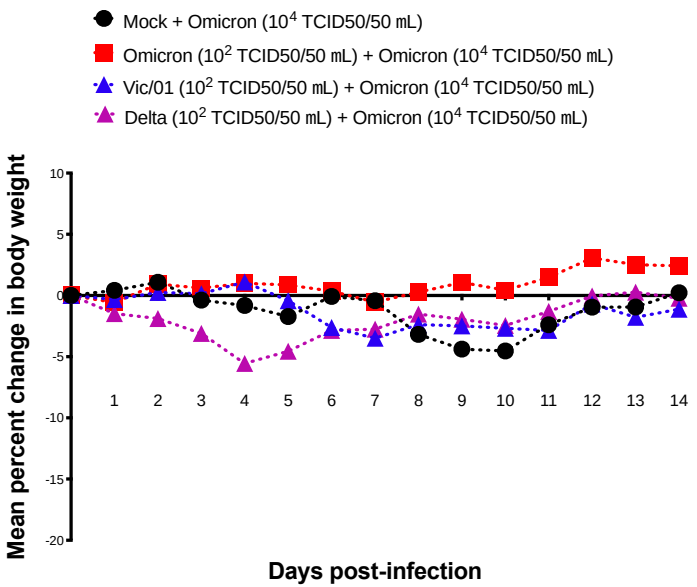


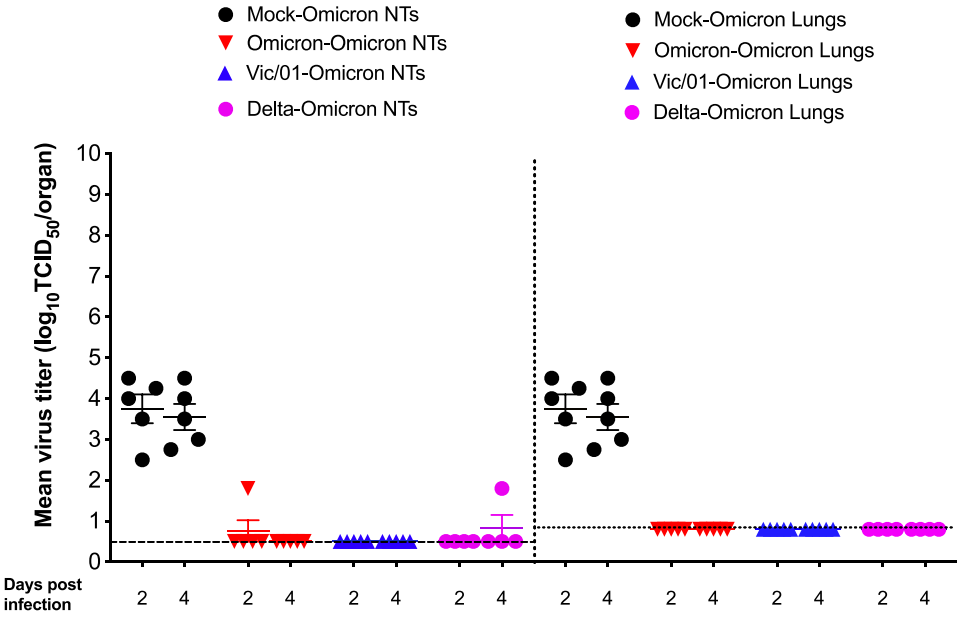
Data from different experiments

Reinfection and cross-challenge with Omicron in K18-hACE2 mice

Low dose primary infection







Homologous and heterologous serum neutralising antibody titres after primary infection

Infecting virus*	Serum NtAb (GMT) against		
	Omicron	Wuhan	Delta
Omicron	**11**	7	8
Wuhan	12	**506**	184
Delta	11	76	**240**

Homologous titre indicated in red font

*Primary infection with low dose of virus: 10^2 $TCID_{50}$ n=5/group

Summary

- Primary Omicron infection in K18-hACE2 mice was not associated with weight loss or mortality, unlike Wuhan and Delta viruses, which caused severe weight loss and mortality.
- Virus titres achieved in the nasal turbinates and lungs following Omicron infection were 1000 to 10,000-fold lower than following Wuhan and Delta virus infections.
- Primary infection with Omicron was poorly immunogenic. Additional serology is pending
- Mice infected with a low dose of Omicron, Wuhan or Delta virus were fully protected from (re)challenge with Omicron.
- Low dose primary infection with Wuhan and Delta viruses induced robust homologous Nt Ab titres with reciprocal cross-reactive Nt Abs (Wuhan vs Delta) but no cross-neutralising Abs detected against Omicron.

Conclusions

- Omicron infection in K18-hACE2 mice is highly attenuated compared with Wuhan and Delta viruses
- Low dose (10^2) primary infection with Omicron does not elicit a neutralising Ab response but mice are protected from rechallenge with a higher dose of Omicron (10^4)
- Low dose (10^2) primary infection with Wuhan and Delta viruses elicits homologous Nt Abs but no heterologous Nt Ab to Omicron. However, Wuhan and Delta convalescent mice were fully protected from challenge with Omicron.

Acknowledements

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