Received: 16 February 2021 | Accepted: 18 February 2021

DOI: 10.1111/resp.14043

CORRESPONDENCE

Official Journal of the Asian Pacific Society of Respirology
Respirology APSR WILEY

Animal models and COVID-19: Mechanism and comorbidities

To the Editors:

I appreciated the recent commentary 'Animal models of COVID-19 hyper-inflammation' by Gantier published in *Respirology*.[1] The author described the importance and potential of animal models, especially mouse models, for the investigation of coronavirus disease 2019 (COVID-19). Dr Gantier touched on the potential for animal models for investigations on the mechanism of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. I would like to add a few points to the discussion.

Mouse models readily enable investigation of immune mechanisms during COVID-19 infection. As described by Gantier, K18-hACE2 mice present a suitable model for the investigation of SARS-CoV-2 infections, as the disease course is very similar to COVID-19.[1] Nevertheless, recent reports have described transfection of hACE2 in both C57BL6 and BALB/c mice,[2] which enables experimental SARS-CoV-2 infection in existing strains of molecule-deficient mice that are already characterized.

These transgenic hACE2 mice could be used to further explore the role of immune receptors and molecules in COVID-19 pathophysiology,[3] and assess the impact of interventions such as blocking antibodies or immune deficiencies in the treatment of aberrant inflammation and cytokine production during SARS-CoV-2 infection.[4]

The use of techniques such as crispr-cas9 and cre lox systems to generate mice with a gene or molecule deletion in specific cells, or tamoxifen cre recombinase induced spatially and temporally defined deletions, will support investigations on cell type-specific responses to COVID-19.

Mouse models will allow scientists to investigate the synergistic effects of different diseases by combining experimental models. Research on the impact of respiratory or metabolic diseases on the development and severity of COVID-19 and the resulting immune responses will facilitate the development of more personalized treatments. These combined models will also aid in the understanding of the impact that COVID-19 represents on the initial comorbidities, as immune activation or tissue damage may aggravate, for example, respiratory functions in chronic obstructive pulmonary disease or glucose metabolism in diabetes mellitus.

Mechanistic investigations and establishment of novel treatments will improve responses to future viral epidemics/pandemics, especially for older people and those with comorbidities. As stated by Dr Gantier, animal models are important in research on the possible long-term effects of the SARS-CoV-2 infection and implications in the immune response to other viruses and bacteria.

While the limitations of animal models are well known, these investigations will be crucial for the prevention and development of more efficient treatments for this and the next viral epidemic/pandemic.

ACKNOWLEDGEMENT

Research funding: Ricardo Wesley Alberca holds a fellowship from Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) grant 19/02679-7.

CONFLICT OF INTEREST

The author declares that he has no conflicts of interest.

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How to cite this article: Alberca RW. Animal models and COVID-19: Mechanism and comorbidities. *Respirology*. 2021;26:616–617. https://doi.org/10.1111/resp.14043