INFECTIOUS DISEASE

SARS-CoV-2 causes COVID-19-like disease in cynomolgus macaquesRockx, B. et al. *Science* <https://doi.org/10.1126/science.abb7314> (2020)

In response to the current pandemic, laboratories all around the world have been racing to produce animal models of SARS-CoV-2 infection. Developing animal models that mimic human disease is a critical step toward the development of COVID-19 therapeutics and vaccines.

Rhesus macaques and ferrets are infectable with SARS-CoV-2, show virus replication and shed virus in nasal swabs. These models are promising candidates for preclinical research but do not fully recapitulate the clinical disease. By showing that SARS-CoV-2 causes COVID-19-like disease in cynomolgus macaques, a study published in *Science* provides an additional model for COVID-19 research.

The investigators led by Bart Haagmans from Erasmus MC inoculated two groups of four cynomolgus macaques with SARS-CoV-2 via a combined intratracheal and intranasal route. Animals were anesthetized for challenge, blood collection, and swabs on different days for up to three

weeks post-inoculation (p.i.). One group was euthanized and autopsied with collection of tissue specimens on day 4 p.i., while the other group was euthanized and autopsied at day 21 p.i.

The macaques showed no overt clinical signs of the disease, but shed virus in nasal and throat swabs. These findings are in accordance with human studies showing that asymptomatic individuals also shed virus. RT-qPCR analysis on day 4 p.i. in different tissues revealed that virus replication was primarily restricted to the respiratory tract. Similar results regarding viral shedding and tissue tropism have been reported in rhesus macaques inoculated with SARS-CoV-2.

At day 4 p.i., two macaques showed macroscopic lesions in the lungs and presented with pathological changes similar to those seen in COVID-19 patients, including alveolar and bronchiolar epithelial necrosis, alveolar edema, hyaline membrane formation and accumulation of immune

cells. Similar to SARS-CoV, SARS-CoV-2 antigen expression was detected in both type I and type II pneumocytes, whereas a separate experiment showed that MERS-CoV antigen was predominantly detected in type II pneumocytes. "Injury to type I pneumocytes can result in pulmonary edema, and formation of hyaline membrane, which may explain why hyaline membrane formation is a hallmark for SARS and COVID-19, but not frequently reported for MERS," explain the investigators in their report.

Although SARS-CoV-2 infection in cynomolgus macaques did not reproduce the respiratory disease seen in rhesus macaques, this study provides a novel model to evaluate preventive and therapeutic measures against SARS-CoV-2 infection.

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