

SYNOPSIS

05/24/2020

Review of “SARS-CoV-2 infection protects against rechallenge in rhesus macaques”

Article citation: Chandrashekar A, Liu J, Martinot AJ, McMahan K, Mercado ND, Peter L, et al. SARS-CoV-2 infection protects against rechallenge in rhesus macaques. *Science*. 2020 May 20 [Epub ahead of print]. Available from: <https://doi.org/10.1126/science.abc4776>

One-Minute Summary

- Using a rhesus macaque model of coronavirus disease 2019 (COVID-19), the authors explored **whether primary infection induces a humoral and cellular immune response protective against reinfection.**
- **Nine adult rhesus macaques in groups of 3 were infected intranasally (IN) and intratracheally (IT)** with 1.1×10^6 plaque forming units (PFUs), 1.1×10^5 PFUs, and 1.1×10^4 PFUs of COVID-19 virus and observed for 35 days.
- After primary infection:
 - Viral replication peaked at day 2.
 - **High viral RNA levels resolved in 10-14 days** in bronchoalveolar lavage (BAL) and in **21-28 days** from nasal swabs (NS) regardless of challenge dose.
 - **Binding and neutralizing antibodies developed regardless of challenge dose**, as well as diverse **antibody-dependent effector functions** (e.g., complement deposition, cellular phagocytosis, neutrophil phagocytosis, NK cell degranulation and cytokine secretion).
 - IFN- γ showed a challenge dose response.
 - CD8+ and CD4+ T cells were induced.
- On day 35, **the 9 macaques were reinfected** with the same dose and route of administration as the primary infection. Three naïve macaques were infected as controls. Compared to the primary infection:
 - **Median peak viral RNA levels were 5 log₁₀ lower in BAL (P < .0001) and NS (P = .0011).**
 - **Rapid anamnestic immune responses were seen in all reinfected macaques** (increased titers of binding antibodies (P = .0034) and two neutralizing antibodies (P = .0003), increased IFN- γ response), despite low levels of viral replication in BAL or NS.
 - Plaque assays with BAL and NS specimens showed no recoverable virus with counts lower than following primary challenge.
 - High viral RNA levels were detected in the challenged naïve rhesus macaques.
- The authors propose that **immunologic means to prevent and treat COVID-19 is possible** but additional research is needed to define the durability of natural immunity.

Additional Information

- Viral RNA was measured by real-time PCR (RT-PCR).
- COVID-19 virus RNA was undetectable in plasma specimens of the infected macaques.
- Four additional rhesus macaques were challenged with 1.1×10^5 PFU of COVID-19 virus by the IN and IT routes and necropsied on day 2 (n=2) and day 4 (n=2).
 - **High levels of viral RNA were detected in the nasal mucosa, pharynx, trachea, and lung tissue** and lower levels were detected in the gastrointestinal tract, liver and kidney.
 - Multifocal regions of acute inflammation and evidence of pneumonia was detected in animals necropsied on day 2 but had diminished in animals necropsied on day 4.
- All challenged rhesus macaques exhibited signs and symptoms suggestive of mild clinical disease but no evidence of severe disease was observed. Further research with a nonhuman model of severe disease is needed.

PHO Reviewer's Comments

None.

Citation

Ontario Agency for Health Protection and Promotion (Public Health Ontario). Review of “SARS-CoV-2 infection protects against rechallenge in rhesus macaques”. Toronto, ON: Queen’s Printer for Ontario; 2020.

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