



It to therapeutic approaches for fighting COVID-19

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Bats are better than humans at mounting an effective immune response against SARS-CoV-2, the virus behind COVID-19. (Marcel Langthim/Pixabay)

Bats are "reservoir hosts" for many coronaviruses, meaning they harbor the pathogens but don't actually develop symptoms of the diseases the viruses cause. Therefore, the immune systems of the winged cave dwellers could offer invaluable insights into how to combat deadly viruses like SARS-CoV-2, the cause of the COVID-19 pandemic. That's the premise behind a new study from researchers at Monash University in Australia.

The researchers reviewed studies of human and bat responses to COVID-19 at three key stages of the disease. They concluded that bats exhibit a "fine-tuned immune response" leading to "only mild and transient inflammation," largely due to differences in how inflammasome activation occurs in them versus in humans. The inflammasome is a complex of proteins in the innate immune system that activates the inflammatory response to pathogens. The researchers **reported** their findings in a review published in the journal *Science Immunology*.

Most immune genes in bats and humans are orthologs, or genes that evolved from common ancestral genes and that maintained their functions over time, the researchers explained. But where bats and people differ is in receptor genes to natural killer, or NK, cells, which are critical in innate defenses against viruses. The receptor genes in bats "potentially decrease the inflammatory cascade" spurred on by the detection of viruses, the researchers said.

This knowledge could point to new strategies for designing COVID-19 therapeutics, the researchers suggested. For example, treatments given at early stages of the disease could focus on boosting type I and III interferon responses in the hopes of ramping up the antiviral response.

But the strategy might change for patients who have developed severe respiratory inflammation, the researchers suggested. Insights from bat immune responses that block inflammasomes suggest that therapeutics that inhibit certain cytokines might be useful. That said, drugs that modulate the immune system "may inadvertently increase viral loads; thus, coadministration of antiviral drugs and/or type I/III [interferons] may mimic the natural immune responses in bats," the researchers wrote.

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Despite the worldwide rollout of vaccines to prevent COVID-19, the emergence of new variants has highlighted the continuing need for treatments that can mitigate severe respiratory distress in patients. Earlier this year, Monash researchers **examined** the role of the microbiome in the immune response to respiratory illnesses. That research led them to suggest that the molecule L-tyrosine might be applicable to treating acute respiratory distress syndrome in COVID-19 patients.

In the newly published review, Monash researchers compared seven classes of COVID-19 remedies that have been studied, and in some cases approved for use in patients, including direct antivirals, like Gilead's **Veklury** (remdesivir), convalescent plasma and kinase inhibitors. They noted that several preclinical and clinical trials of dozens of drug treatments for the virus are ongoing and that the field "will continue to evolve."

The scientists also noted knowledge about bats' immune responses to coronaviruses has revealed gaps in research. For example, the biology behind the ability of SARS-CoV-2 to evade the human immune system is still not well understood, they said. And much more could be done to detail the potential interactions between SARS-CoV-2 and the microbiome, they added.

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