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COVID-19 infection can be inhibited by elements of the human microbiome

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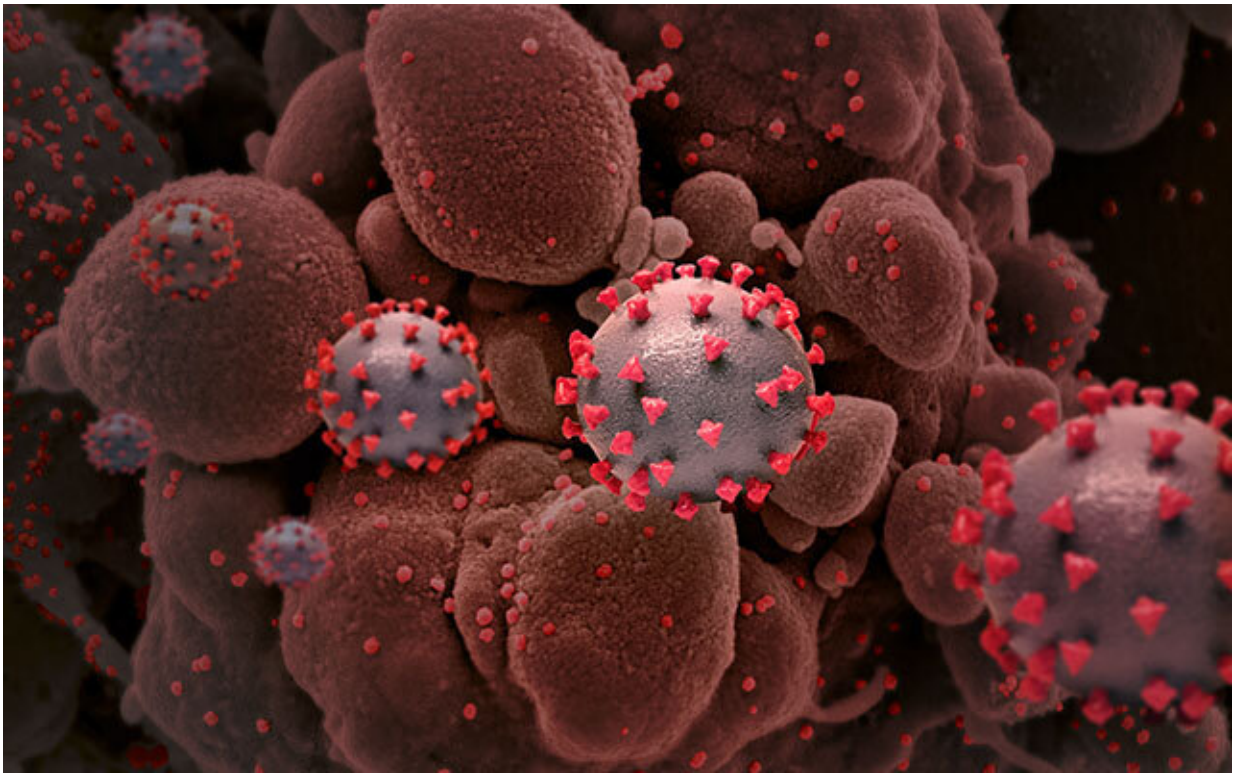

Creative rendition of SARS-CoV-2 particles (not to scale). Credit: National Institute of Allergy and Infectious Diseases, NIH

In the human microbiome, researchers have identified metabolites (intermediate or end products of metabolism) that inhibit COVID-19 infection in cell-based models of the virus. The finding, reported this

week in the journal *mSphere*, an open-access journal of the American Society for Microbiology, is yet another example of the wealth of information that can be gained by studying the human microbiome, the collection of microbes, bacteria, fungi and viruses that live on and inside the human body. The finding may also help in the development of new therapeutics that can battle COVID-19 infections.

"We have found that bacteria that grow on and in you make specific molecules that can inhibit, at least in a laboratory setting, the cell-based viral infection of SARS-CoV-2, and the molecules appear to do that by a number of different mechanisms," said study principal investigator Sean Brady, Ph.D., professor and head of the Laboratory of Genetically Encoded Small Molecules, at the Rockefeller University, New York City.

Brady said the COVID-19 pandemic has highlighted the need to identify additional antiviral small molecules to complement existing therapies. While increasing evidence suggests that metabolites produced by the human microbiome have diverse biological activities affecting the human host, there is comparatively little information on the metabolites' antiviral properties.

In the new study, Brady and colleagues used a cell-based SARS-CoV-2 infection assay to screen metabolites from a sample of bacteria from the human microbiome. They identified 3 bacterial metabolites capable of inhibiting SARS-CoV-2 infection: An adenosine analog, tryptamine and a disubstituted pyrazine.

The identified molecules display structural similarities to synthetic drugs that have been explored for the treatment of COVID-19. "It was intriguing that of all the chemistries available, the metabolites we uncovered from the microbiome all bore similarities to clinically-relevant antivirals," said Frank Piscotta, Ph.D., lead author on the study

and a post-doc in the Laboratory of Genetically Encoded Small Molecules.

The researchers say these molecules could serve as starting points for the development of new antivirals. In addition, researchers could deliver the antiviral-producing bacteria as a therapeutic intervention. The researchers say they want to study the mechanisms by which the metabolites function and whether the bacteria producing these molecules have any effect on viral infection upon colonization of an animal. As more data becomes available, they also plan to examine whether the presence or absence of these antiviral-producing bacteria in humans can be linked to severity of viral infection.

"Our discovery of structurally diverse metabolites with anti-SARS-CoV-2 activity from screening a small fraction of the bacteria reported to be associated with the human microbiome suggests that continued exploration of phylogenetically diverse human-associated bacteria is likely to uncover additional small molecules that inhibit SARS-CoV-2 as well as other viral infections," said Brady.

Brady says this is one of the first studies to show that molecules produced by the human microbiome can inhibit viral infections, particularly of coronaviruses like SARS-CoV-2.

More information: Frank J. Piscotta et al, Metabolites with SARS-CoV-2 Inhibitory Activity Identified from Human Microbiome Commensals, *mSphere* (2021). DOI: 10.1128/mSphere.00711-21

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