Study shows inexpensive, readily available chemical may limit impact of COVID-19

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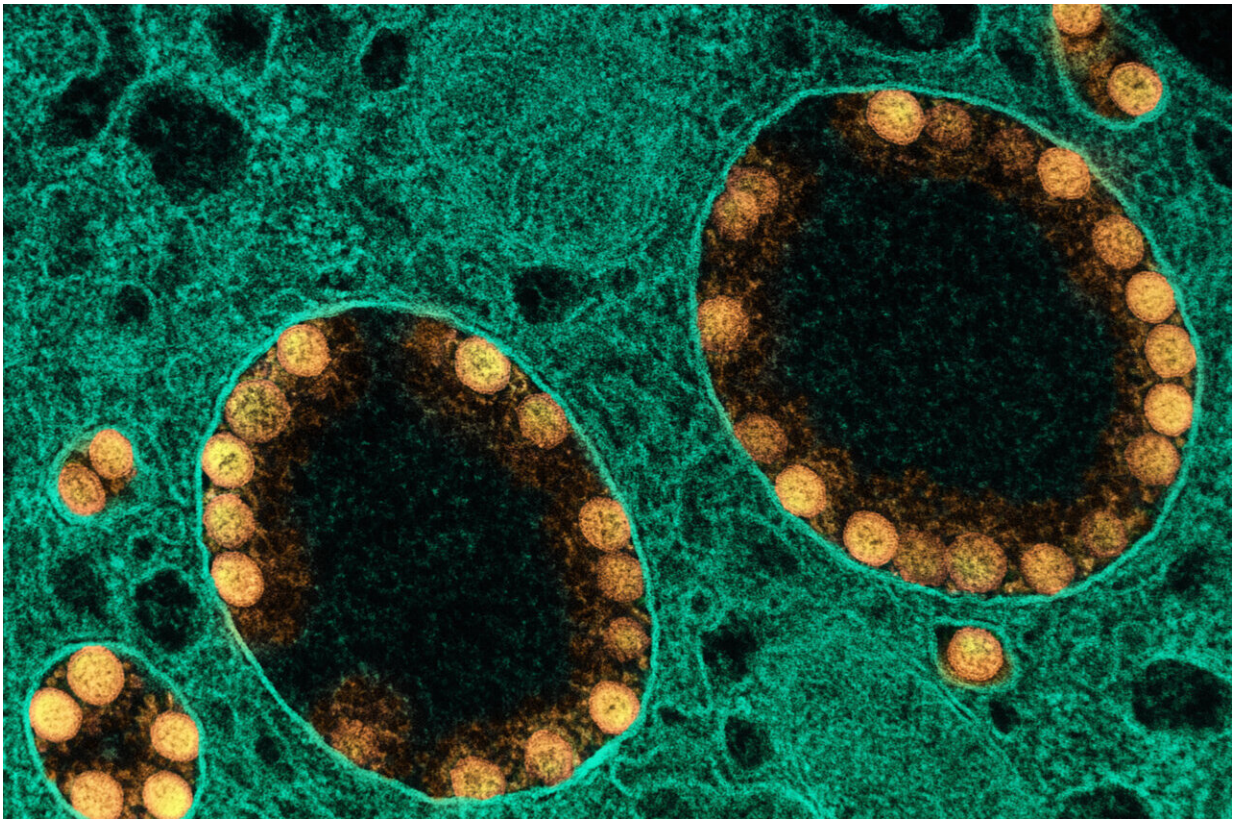

Transmission electron micrograph of SARS-CoV-2 virus particles (colored yellow) within the endosomes of a heavily infected nasal olfactory epithelial cell. Credit: NIAID

Preclinical studies in mice that model human COVID-19 suggest that an inexpensive, readily available amino acid might limit the effects of the

disease and provide a new off-the-shelf therapeutic option for infections with SARS-CoV-2 variants and perhaps future novel coronaviruses.

A team led by researchers at the David Geffen School of Medicine at UCLA report in *Frontiers in Immunology* that an amino acid called GABA, which is available over-the-counter in many countries, reduced disease severity, viral load in the lungs, and death rates in SARS-CoV-2-infected mice. This follows up on their previous finding that GABA consumption also protected mice from another lethal mouse coronavirus called MHV-1. In both cases, GABA treatment was effective when given just after infection or several days later near the peak of virus production. The protective effects of GABA against two different types of coronaviruses suggest that GABA may provide a generalizable therapy to help treat diseases induced by new SARS-CoV-2 variants and novel beta-coronaviruses.

"SARS-CoV-2 variants and novel coronaviruses will continue to arise, and they may not be efficiently controlled by available vaccines and antiviral medications. Furthermore, the generation of new vaccines is likely to be much slower than the spread of new variants," said senior author Daniel L. Kaufman, a researcher and professor in Molecular and Medical Pharmacology at the David Geffen School of Medicine at UCLA. Accordingly, new therapeutic options are needed to limit the severity of these infections. Their previous studies showed that GABA administration protected mice from developing severe disease after infection with a mouse coronavirus called MHV-1. To more stringently test the potential of GABA as a therapy for COVID-19, they studied transgenic mice that when infected with SARS-CoV-2 develop severe pneumonia with a high mortality rate. "If our observations of the protective effects of GABA therapy in SARS-CoV-2-infected mice are confirmed in clinical trials, GABA could provide an off-the-shelf treatment to help ameliorate infections with SARS-CoV-2 variants. GABA is inexpensive and stable at room temperature, which could make

it widely and easily accessible, and especially beneficial in developing countries."

The researchers said that GABA and GABA receptors are most often thought of as a major neurotransmitter system in the brain. Years ago, they, as well as other researchers, found that cells of the immune system also possessed GABA receptors and that the activation of these receptors inhibited the inflammatory actions of immune cells. Taking advantage of this property, the authors reported in a series of studies that GABA administration inhibited autoimmune diseases such as type 1 diabetes, multiple sclerosis, and rheumatoid arthritis in mouse models of these ailments.

Other scientists who study gas anesthetics have found that lung epithelial cells also possess GABA receptors and that drugs that activate these receptors could limit lung injuries and inflammation in the lung. The dual actions of GABA in inflammatory immune cells and lung epithelial cells, along with its safety for clinical use, made GABA a theoretically appealing candidate for limiting the overreactive immune responses and lung damage due to coronavirus infection.

Working with colleagues at the University of Southern California, the UCLA research team in this study administered GABA to the mice just after infection with SARS-CoV-2, or two days later when the virus levels are near their peak in the mouse lungs. While the vast majority of untreated mice did not survive this infection, those given GABA just after infection, or two days later, had less illness severity and a lower mortality rate over the course of the study. Treated mice also displayed reduced levels of virus in their lungs and changes in circulating immune signaling molecules, known as cytokines and chemokines, toward patterns that were associated with better outcomes in COVID-19 patients. Thus, GABA receptor activation had multiple beneficial effects in this mouse model that are also desirable for the treatment of

COVID-19.

The authors hope that their new findings will provide a springboard for testing the efficacy of GABA treatment in clinical trials with COVID-19 patients. Since GABA has an excellent safety record, is inexpensive and available worldwide, clinical trials of GABA treatment for COVID-19 can be initiated rapidly.

The authors also suspect that the anti-inflammatory properties of GABA-receptor activating drugs may also be useful for limiting inflammation in the central nervous system that is associated with long-COVID. Indeed, this approach was very successful in their previous studies of therapeutics for multiple sclerosis in mice, a disease which is caused by an inflammatory autoimmune response in the brain. The authors speculate that such drugs may reduce both the deleterious effects of coronavirus infection in the periphery and limit inflammation in the central nervous system.

Unfortunately, there has been no pharmaceutical interest pursuing GABA therapy for COVID-19, presumably because it is not patentable and widely available as a dietary supplement. The authors hope for federal funding to continue this line of study.

The researchers emphasize that unless clinical trials are conducted and GABA is approved for treating COVID-19 by relevant governing bodies, it should not be consumed for the treatment of COVID-19 since it could pose health risks, such as dampening beneficial immune or physiological responses.

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More information: A GABA-receptor agonist reduces pneumonitis severity, viral load, and death rate in SARS-CoV-2-infected mice, *Frontiers in Immunology* (2022). DOI: 10.3389/fimmu.2022.1007955

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