

Preclinical study suggests new approach to reduce COVID-19 death among the elderly

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New research from the University of Minnesota Medical School and colleagues at the Mayo Clinic reveals a possible new approach to preventing death and severe disease in elderly people infected with

SARS-CoV-2.

The researchers demonstrated in a [preclinical study](#) that senolytic drugs significantly reduced [mortality](#) upon infection from a beta-coronavirus closely related to SARS-CoV-2 in older mice. The study published in *Science* was co-led by Laura Niedernhofer, MD, Ph.D. and Paul Robbins, Ph.D., both professors in the Department of Biochemistry, Molecular Biology and Biophysics and co-directors of the Institute on the Biology of Aging and Metabolism at the U of M Medical School, and Sara Hamilton, Ph.D., assistant professor in the Department of Laboratory Medicine and Pathology.

Senescent [cells](#)—which are cells in the body that are damaged—contribute to inflammation, multiple chronic diseases and age-related loss of resilience, and they accumulate in our body as we age. Senolytic drugs, previously co-discovered by the U of M Medical School and the Mayo Clinic researchers, selectively remove [senescent cells](#) from the body.

The COVID-19 pandemic has revealed the pronounced vulnerability of the elderly and chronically-ill to morbidity and mortality induced by SARS-CoV-2. The research team sought to discover why older people are more vulnerable to these adverse outcomes. The team hypothesized it was senescent cells and removing them with senolytics would dial back inflammation and enable an improved response to viral infection.

"We wanted to determine if therapeutically targeting fundamental aging mechanisms, such as cellular senescence, could reduce morbidity and mortality following viral infection," said Christina Camell, Ph.D., an assistant professor in the Department of Biochemistry, Molecular Biology and Biophysics, and a first author of the study.

The researchers found that older mice exposed for the first time to a

mouse beta-coronavirus experienced nearly 100% mortality, whereas young mice barely got sick. When they treated the older mice with senolytic drugs following infection, their survival rate increased to 50%. The senolytic drugs reduced mortality, cellular senescence and inflammatory markers and increased anti-viral antibodies.

"We have been working on a new approach to help the elderly remain healthy, which is to find therapeutics to treat aging rather than treating each individual disease associated with old age. The fact that senolytics worked to protect old organisms from a viral infection proves that approach is accurate," Robbins said. "By getting rid of a piece of aging biology, senescent cells, with senolytics, the older mice were able to withstand the stress of [infection](#). This suggests that reducing the burden of senescent cells in ill or elderly individuals could improve their resilience and reduce their risk of dying from COVID-19."

These results in mice supported the initiation of two clinical trials to reduce mortality in elderly COVID-19 patients. The team also plans to study if senescent cells contribute to the long-hauler effect in many COVID-19 survivors.

More information: Christina D. Camell et al, Senolytics reduce coronavirus-related mortality in old mice, *Science* (2021). [DOI: 10.1126/science.abe4832](https://doi.org/10.1126/science.abe4832)

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