

Long-term benefits of 'senolytic' drugs on vascular health in mice

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Building on previous studies, Mayo Clinic researchers have demonstrated significant health improvements in the vascular system of mice following repeated treatments to remove senescent cells. They say this is the first study to show that regular and continual clearance of senescent cells improves age-related vascular conditions - and that the method may be a viable approach to reduce cardiovascular disease and death. The findings appear online in *Aging Cell*.

"Cardiovascular disease remains the leading cause of death in our population today, and disability related to heart disease and stroke has a tremendous impact on our aging population," says James Kirkland, M.D., Ph.D., director of the Robert and Arlene Kogod Center on Aging at Mayo Clinic and co-corresponding author of this study. "This is the first evidence that longer term use of senolytic drugs to clear these damaged cells from the body can have a preventative impact against vascular diseases."

Senescent cells are damaged cells that no longer function properly, but remain in the body and contribute to frailty and many of the other health conditions associated with aging. Prior studies at Mayo showed chronic removal of the cells from genetically-altered [mice](#) can alter or delay many of these conditions, and short-term treatment with drugs that remove senescent cells can improve the function of the [endothelial cells](#) that line the blood vessels. This study, however, looked at the structural and functional impacts of cell clearance using a unique combination of drugs on blood vessels over time. Mice were 24 months old when the

drugs - a cocktail of dasatinib and quercetin - were administered orally over a three-month period following those initial two years. A separate set of mice with high cholesterol was allowed to develop atherosclerotic plaques for 4 months and were then treated with the drug cocktail for two months.

The research showed that senescent cell clearance in either naturally-aged or atherosclerotic mice alleviated vascular dysfunction. Although it did not reduce the size of plaques in mice with [high cholesterol](#), it did reduce calcification of existing plaques on the interior of vessel walls.

"Our finding that senolytic drugs can reduce cardiovascular calcification is very exciting, since [blood vessels](#) with calcified plaques are notoriously difficult to reduce in size, and patients with heart valve calcification currently do not have any treatment options other than surgery," says Jordan Miller, Ph.D., Mayo cardiovascular surgery researcher and senior author of the paper. "While more research is needed, our findings are encouraging that one day removal of [senescent cells](#) in humans may be used as a complementary therapy along with traditional management of risk factors to reduce surgery, disability, or death resulting from [cardiovascular disease](#)."

Provided by Mayo Clinic

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