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Researchers demonstrate senescent cell burden is reduced in humans by senolytic drugs

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In a small safety and feasibility clinical trial, Mayo Clinic researchers have demonstrated for the first time that senescent cells can be removed from the body using drugs termed "senolytics". The result was verified not only in analysis of blood but also in changes in skin and fat tissue senescent cell abundance. The findings appear in the journal *EBioMedicine*.

This trial—involving participants who had diabetes-related kidney disease—is the second clinical study of senolytics to be published by Mayo, but is the first trial to show that senolytic drugs, discovered by Mayo researchers, can remove senescent cells from humans as they did in numerous studies in animals.

Senescent cells are malfunctioning cells that accumulate with aging and in organs affected by chronic diseases. Senescent cells can remain in the body and contribute to multiple diseases as well as features of aging, ranging from heart disease to frailty, dementias, osteoporosis, diabetes, and kidney, liver, and lung diseases.

"Senescent cells can develop in all mammals in response to disease, injury, or cancerous mutations. Senolytic drugs do not interfere with generation of senescent cells, which could lead to cancer. However, once formed, senescent cells can contribute to developing cancers, multiple other diseases, and consequences of aging," says James Kirkland, M.D.,

Ph.D., senior author and head of the Robert and Arlene Kogod Center on Aging.

"By targeting senescent cells with senolytics in mice, we can delay, prevent, or treat multiple diseases and increase health and independence during remaining years of life," says Dr. Kirkland. "As we increase our understanding of these drugs and their effects, we hope there may be benefits for a range of human diseases and disorders."

For three days the nine participants received a combination dose of dasatinab and quercetin. Though the drugs cleared the body in a couple of days, effects on reducing senescent cells were evident for at least 11 days. The researchers say this shows the senolytic drug combination significantly decreases senescent cell burden in humans. Senescent cells are characteristic in end-stage kidney failure as well as diabetes-related kidney disease. By removing the cells from mice, researchers had previously found that senolytics alleviate insulin resistance, cell dysfunction, and other processes that cause disease progression and complications.

While more research is needed on the impact of senolytics on diseases and disorders of aging, the researchers say the results of occasional dosing reduces risks from having to give drugs continuously.

"This small-scale clinical trial is a significant step forward for translation of senolytic therapies," says Ronald Kohanski, Ph.D., deputy director, Division of Aging Biology, National Institute of Aging. "The demonstration that senescent cell numbers can be reduced in two tissues in humans is an important advance based on the compelling evidence from studies in laboratory mice."

Provided by Mayo Clinic