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COVER STORY

Removal of Senescent Cells "Might Transform Medicine"

By William Faloon

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On **July 9, 2018**, the world awoke to news from the **Mayo Clinic** that many age-related afflictions can be reversed by eliminating **senescent cells** from old mice.[1]

In addition to regaining aspects of youthful health, the old mice whose **senescent cells** were selectively removed lived **36% longer**.[1]

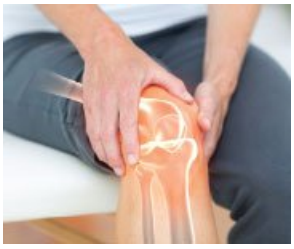
This is not the first study showing these effects. What makes it exceptional is the meticulous way it was conducted.

The first part of the study involved transplanting a few **senescent cells** into **young** mice. This caused the young mice to endure physical decline characteristic of degenerative aging. When senescent cells were transplanted into old mice, the same toxic effects occurred and the mice died sooner.

But with **oral** administration of compounds that remove **senescent cells**, physical dysfunction was alleviated and lifespan markedly increased.

The incredible news is that novel ways are being developed to help remove **senescent cells** from aging **humans** today!

Why Senescent Cells Accumulate



As cells age, most undergo a beneficial **elimination** process known as **apoptosis**.

If all aged cells properly **self-eliminated**, we would see improvements in healthy lifespans.[2]

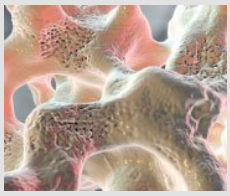
Instead, too many **senescent cells** linger. These aged cells emit ***signals*** that promote inflammation, injure healthy cells, and block regenerative factors that may improve one's health.[3]

This scenario occurs inside our bodies, whereby **senescent cells** fail to undergo **apoptosis** (normal cell elimination). These pesky **senescent cells** emit inflammatory-type signals that spread to **healthy cells** and cause them to deteriorate.

SENOLYTICS EXTEND HEALTHY LIFESPAN

Rodent study shows senolytics

dasatinib + quercetin:



Osteoporosis

- Improve frailty symptoms (gait, grip strength)
- Enhance hair color appearance
- Improve cardiac/arterial function
- Reduce tremors and urinary incontinence
- Decrease osteoporosis
- Increase exercise endurance
- Improve kidney/liver age scores
- Extend healthy lifespan

Does anyone NOT want these benefits?

Aging Cell. 2015 Aug;14(4):644-58. doi: 10.1111/acel.12344. Epub 2015 Apr 22.

An Old Problem with New Solutions

I was informed about **senescent cells** in the late **1990s** by a brilliant researcher. He made it clear that if we were to achieve meaningful control over **aging**, we had to **selectively** remove **senescent cells** that accumulate and create metabolic havoc.

The problem back then was there was no valid approach to accomplish this.

Starting around year **2014,** scientists at the **Mayo Clinic** and **Scripps Research Institute** began investigating **senolytics**, which are compounds that induce normal elimination of **senescent cells**.[4]

Remarkable Results

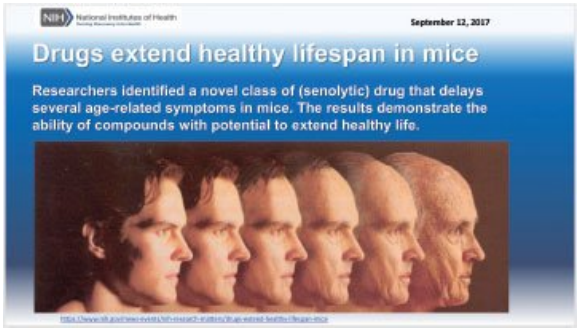
The box on the previous page is from a presentation I give to advocate for accelerated **age-reversal** research. This slide highlights findings from a groundbreaking (year 2015) animal study that found remarkable **rejuvenation** effects in response to aggressive **senolytic** therapy.

This **2015** study[4] was followed by another study funded in part by the **National Institutes of Health** (NIH) published in 2017.[5]

The **2017** study looked at age-accelerated mice treated with a **senolytic** compound. The findings showed **improvements** in grip strength, coat condition, movement, and overall health. This study also revealed improvement in a biomarker of senescent cells in the **kidney** compared with control mice.[5]

Favorable Media Coverage

These studies generated worldwide headlines, with scientists describing the potential of **senolytic** compounds to reverse **aging** in humans.



In a review published by **The American Geriatrics Society** (2017), **senolytics** were described as having potential to:

> "…transform geriatric medicine by enabling prevention or treatment of multiple diseases and functional deficits in parallel, instead of one at a time."[2]

The authors of this review explained how reducing the "***senescent cell burden***" can lead to less **inflammation** with enhanced function of **stem cells**.[2]

The review went on to describe how **senescent cells** destroy the **knee joints** of healthy mice.[6] These findings have encouraged people with **osteoarthritis** to self-experiment with **senolytic** compounds, with encouraging results being reported.

Of interest is that **senolytics** do not have to be used continuously to derive benefits. This corroborates current strategies whereby people are using senolytics **intermittently** ("on" and "off" periods).

This **2017** review concluded that after clinical trials are completed:

> "…it is conceivable that the rapidly emerging repertoire of senolytic agents might transform medicine as we know it."[2]

Researchers have further remarked that the introduction of **senolytics** into clinical practice could be **transformative** when stating:

> "Our goal is to achieve the same success in humans as we have in preclinical animal models in efforts to prevent or delay the conditions associated with aging."[7]

Human senolytic studies are being pursued by a number of physician/scientists. We look forward to reporting on them after more long term data is gathered.

Practical Senolytic Approaches

Early stage research on senolytics indicates that **intermittent** dosing may be an ideal approach. In other words, the strategy is to selectively induce senescent cell **apoptosis** for a **limited** time, and then **cease** until more **senescent cells** accumulate.

Drugs that purge senescent cells are being clinically studied. Some individuals are self-experimenting today with **senolytic drugs** + high-dose **quercetin**.

In a cell culture study, the drug **dasatinib** eliminated human senescent **fat cell** progenitors.[4] **Quercetin** was more effective against senescent human

endothelial cells and **bone marrow stem cells**.[4]

Improving **circulation** via enhanced **endothelial function** and enabling more potential **stem cell** release from bone marrow is important. Removing **fat-cell** progenitors is desirable, since these cells can negatively impact surrounding tissue and are linked to metabolic dysfunction.[8]

Until recently, people seeking to achieve **senolytic** benefits were challenged to take large-doses of **quercetin**, and many don't yet want to try **dasatinib**. A new **quercetin phytosome** eliminates the need to ingest large amounts of quercetin.

Another discovery suggests that a tea extract containing **theaflavins** provides some of the same **senolytic** properties targeted by **dasatinib**,[9-11] and other senolytic drugs.[12]

How to Purge Senescent Cells Today

A new **quercetin phytosome** provides approximately **50 times** greater oral bioavailability compared to typical quercetin supplements.[13]

This enables **74 mg** of this **quercetin phytosome** (providing **25 mg** quercetin) to deliver a dose approximately equivalent to about **1,250 mg** of typical quercetin. This empowers more people to achieve greater amounts of intact and unmodified **quercetin** into their bloodstream.

In addition to having a similar mechanism of action as dasatinib,[9-11] preclinical evidence indicates the senolytic potential of black tea **theaflavins**.[14] Based on our interpretation of the current research findings, we suggest most people over age 35 consider taking a once **weekly** dose of:

- **74 mg** of **quercetin phytosome**
- **275 mg** of **theaflavins**

Those taking lower doses of regular **quercetin** for its other benefits may continue to do so and use the new **phytosome delivery** formula on an **intermittent** schedule. The article on page 6 of this issue describes this **low-cost** and novel approach to removing **senescent cells** by taking **theaflavins** and **quercetin phytosome** just one time each week.

The cost of this once-weekly senolytic nutrient approach is less than **$7** a month.

Restore Youthful Circadian Sleep Patterns

Aging and erratic lifestyle disrupts our ability to retain **circadian** balance via restorative **sleep**.

Healthy **circadian rhythm** function is reliant on expression of **genes** that **"turn on"** vital ***signaling*** pathways throughout the body. It's why we often feel "systemically" terrible when we suffer a night of broken sleep or insomnia.

A **citrus-peel** extract containing **nobiletin** has been shown to restore **circadian gene expression** in mice. An article on page 38 of this issue describes how people with disrupted circadian rhythms may derive benefit.

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For longer life,

William Faloon, Co-Founder
Life Extension Buyers Club

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