

# Clinical Trials Corner

Dear Readers,

Welcome to the Clinical Trials Corner of *Nutrition and Healthy Aging*. The aim of this section is to inform readers of upcoming clinical trials and highlight new findings. Please email if you would like to draw attention to a specific topic or upcoming clinical trial; leonie.heilbronn@adelaide.edu.au

Cellular senescence is a process in which damaged cells persist in a pro-inflammatory and pro-fibrotic state, rather than being targeted for degradation. Cellular senescence is linked to aging related disease and physical dysfunction in mice [1] and is reduced by calorie restriction [2].

Senolytic compounds that selectively induce death in senescent cells are being explored for their anti-aging properties. Intermittent treatment of aged mice with dasatinib plus quercetin (DQ) for 4 months increased speed, endurance and grip strength as compared to vehicle [1].

In a non-placebo controlled trial, intermittent DQ treatment improved walking distance and gait speed during the 6-minute walk test and chair-stands in 14 older humans with idiopathic pulmonary fibrosis over 3 weeks [3]. There was no change in grip strength or pulmonary function, and some mild to moderate side effects were reported, such as respiratory symptoms, headaches and gastrointestinal discomfort.

Naturally occurring compounds are currently being explored for their senolytic potential. Fisetin, a flavenol that is found in high concentrations in many fruits and vegetables, is known to have anti-inflammatory, antioxidant, neuroprotective and cardioprotective effects in animals. Recently, fisetin was shown to have higher senolytic potential over other flavonoids including luteolin, curcumin and quercetin in fibroblasts [4]. Furthermore, administration of fisetin to wild type mice reduced cellular senescence, aging related pathologies and increased maximal lifespan [4].

Researchers at the Mayo Clinic are currently conducting two double blind randomised controlled trials to test the effects of fisetin in older individuals. In one study, 70–90 year old women will be examined to compare effects on markers of frailty, inflammation, insulin resistance and bone health over 2 months. The second study will examine both men and women in this age range with the primary outcome to reduce inflammation.

We await completion of these pilot trials to ascertain the safety and therapeutic potential of fisetin, which could lead to development of larger clinical trials examining effectiveness of this compound to improve aging related dysfunction.

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## References

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- [2] Wang C, Maddick M, Miwa S, Jurk D, Czapiewski R, Saretzki G, Langie SA, et al. Adult-onset, short term dietary restriction reduces cell senescence in mice. *Aging*. 2010;2(9):555-66.
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- [4] Yousefzadeh MJ, Zhu Y, McGowan SJ, Angelini L, Fuhrmann-Stroissnigg H, Xu M, Ling YY, Melos KI, Pirtskhalava T, Inman CL, McGuckian C, Wade EA, Kato JI, Grassi D, Wentworth M, Burd CE, Arriaga EA, Ladiges WL, Tchkonian T, Kirkland JL, Robbins PD, Niedernhofer LJ. Fisetin is a senotherapeutic that extends health and lifespan. *EBioMedicine*. 2018;36:18-28.

<https://www.clinicaltrials.gov/>

**A). Study Title:** AFFIRM: A Phase 2 Randomized, Placebo-Controlled Study of Alleviation by Fisetin of Frailty, Inflammation, and Related Measures in Older Women

**Clinicaltrials.gov identifier:** NCT03430037

**Sponsor:** Mayo Clinic

**Primary Outcome:** Improved 6 minute walk [Time Frame: One Month]

**Secondary Outcomes:** not listed

**B). Study Title:** AFFIRM-LITE: A Phase 2 Randomized, Placebo-Controlled Study of Alleviation by Fisetin of Frailty, Inflammation, and Related Measures in Older Adults

**Clinicaltrials.gov identifier:** NCT03675724

**Sponsor:** Mayo Clinic

**Primary Outcome:** Decrease in blood inflammation markers [Time Frame: Seven days].

**Secondary Outcomes:** not listed