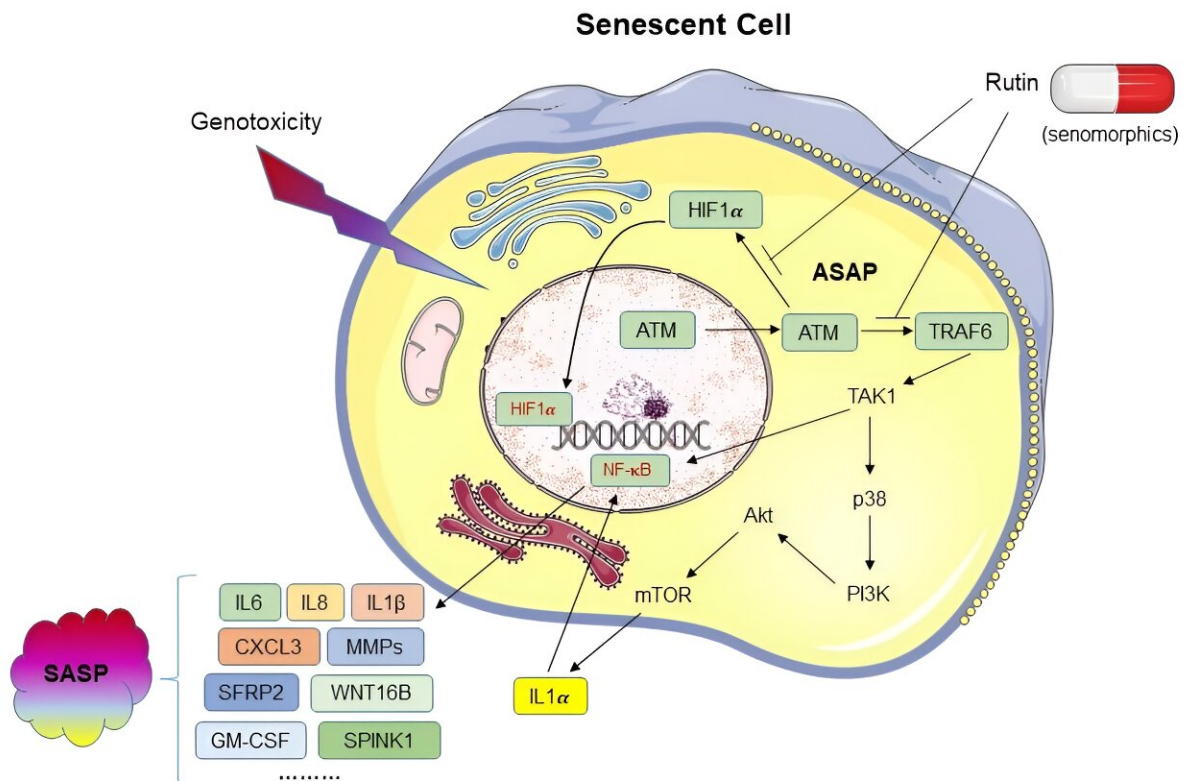


# Novel senomorphic agent of natural origin found to target aging

July 31 2023, by Chen Na



The intracellular mechanisms that support Rutin to function as a novel senomorphic agent in antiaging interventions. Credit: Dr. SUN's group

Since the discovery of hallmark features of senescence such as cell cycle arrest, apoptosis resistance and development of a senescence-associated

secretory phenotype (SASP), efforts in understanding how senescent cells drive physiological and pathological aging have grown exponentially. The accumulation of senescent cells in aging individuals is associated with increased occurrence of age-associated pathologies that contribute to poor health, frailty, and mortality.

Targeting [senescent cells](#) with senolytics or senomorphics hold the potential to mitigate the vast majority of age-related disorders. Examples of senopathies include but are not limited to neurodegenerative, cardiovascular, metabolic, musculoskeletal, liver, lung and kidney diseases.

However, the major challenge in developing novel senotherapies is the paucity of antiaging agents that have decent safety profiles, a condition that limits development of many pharmacological pipelines.

Prof. Sun Yu and his colleagues at Shanghai Institute of Nutrition and Health, Chinese Academy of Sciences recently performed large scale screening of a natural medicinal agent library for senotherapeutic candidates and validated several agents, which showed their excellent potential to serve as senomorphics. The study, titled "Rutin is a potent senomorphic agent to target senescent cells and can improve chemotherapeutic efficacy," was published online in *Aging Cell* on July 20, 2023.

Rutin, a small molecule phytochemical component enriched in an array of plants, exhibited an outstanding capacity in targeting senescent cells by reducing the expression of a full spectrum SASP.

In-depth investigation revealed that Rutin mainly curtails the acute stress-associated phenotype (ASAP) by specifically abrogating the interaction between ATM and HIF1 $\alpha$ , as well as the interaction between ATM and TRAF6, critical events that together underlie the ASAP development

until the phenotype culminates in the form of a typical SASP.

Such a mechanism allows Rutin to effectively control the impact of senescent cells in generating a highly pro-inflammatory extracellular microenvironment, which frequently promotes the incidence and exacerbation of many age-related diseases in the advanced life stage of humans.

Preclinical data of Sun's lab suggested that Rutin has an excellent efficacy in promoting chemotherapeutic outcomes, such as in the case of mitoxantrone treatment. Although [cancer cells](#) also become senescent in response to various chemotherapeutic regimens, they cannot repopulate and expand continuously within tumor foci during and/or after anticancer regimens. However, stromal cell subpopulations tend to become senescent in response to anticancer treatments, and confer surviving cancer cells with remarkable resistance to [anticancer drugs](#).

For this reason, senolytics and/or senomorphics are increasingly proposed as adjuvant treatments to deplete senescent cells in vivo. As effective SASP inhibitors, senomorphic agents such as Rutin can be used as ideal alternatives to senolytics, as they preserve the less SASP-dependent pro-immunogenic capacity of [senescent cells](#), particularly tumor immunosurveillance in the context of cancer cell survival.

This study provides a proof of concept for Rutin as an emerging natural senomorphic agent, and demonstrates an effective therapeutic modality in mitigating age-related pathologies, including but not limited to various malignancies.

"We hope that our study opens a new window, through which people are able to envision the possibility of discovering more antiaging drugs of natural origin, particularly from [plant species](#), and make informed decisions about their lifespan-extending regimens," Dr. Sun said.

**More information:** Hanxin Liu et al, Rutin is a potent senomorphic agent to target senescent cells and can improve chemotherapeutic efficacy, *Aging Cell* (2023). [DOI: 10.1111/ace.13921](https://doi.org/10.1111/ace.13921)

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