

2023

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Recommended Citation

Aldridge, Kristin (2023) "Do Sleeper Cells Hold the Key to Immortality? Senescent cells in cancer and aging," *The Synapse: Intercollegiate science magazine*: Vol. 35: Iss. 1, Article 6.
Available at: <https://digitalcommons.denison.edu/synapse/vol35/iss1/6>

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Do Sleeper Cells Hold the Key to Immortality?

Senescent cells in cancer and aging.

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Illustrated by Orion Pendley

All organisms experience life and death, but what if you could find a way to shut down for a few years and wake up the same age and with the same memories as you had before? This is what senescent cells do. Senescent cells stop multiplying but remain viable, essentially “going to sleep,” sometimes for years, to be reactivated in the future. Some researchers believe senescent cells hold the secret to immortality and longevity. Others seek ways to use them in cancer research. The field is just starting to develop, and the possible implications senescence could hold for the future of human healthcare is ever expanding.

Senescence cells were discovered in 1961 by doctors, Leonard Hayflick and Paul Moorhead of the Wistar Institute of Anatomy and Biology in Philadelphia, Pennsylvania. Dr. Hayflick and Moorhead discovered it when the serially subcultured human embryonic fibroblasts (connective tissue cells) they were working with lost the ability to replicate but were still viable. They termed these “senescent” cells. Very quickly, two hypotheses emerged about their discovery. The first is that these cells are anti-cancer and tumor-suppressive. Activities such as DNA damage caused by chemotherapies can move cells into senescence, eliminating the chance of uncontrolled cell proliferation (a hallmark of tumor growth) and decreasing the chance of accumulating gene mutations. The second hypothesis is that these cells are pro-aging. Since tissue regeneration slows down as we age and cellular repair decreases, they determined that the accumulation of senescent cells was the reason for this. Over time, these two schools of thought came together to create an overarching picture of cellular senescence and how it can be harnessed to better human healthcare.

The accumulation of senescent cells has also been correlated with aging, and the pro-inflammatory secretome may play a part in many age-related disease.

Cell senescence during tumor formation sounds ideal, but unfortunately, these cells continue releasing chemicals that trigger inflammation, a common indication of cancer. The accumulation of senescent cells has also been correlated with aging, and the pro-inflammatory secretome may play a part in many age-related diseases such as osteoporosis, cardiovascular disease, and declines in eyesight, mobility, and thinking ability. Being able to eradicate these cells after they reach senescence would be an ideal treatment in addition to the chemotherapies and radiation that patients typically receive. It would also help reduce the accumulation and risk of diseases in aging patients.

So, how can we use senescent cells to our benefit without incurring their risks? The key to this is what research scientists are calling the “one-two-punch” treatment. For people with cancer, first hit the tumor cells with radiation and chemotherapy (first punch), then hit the tumor again with senotherapeutic compounds, which are compounds created to kill senescent cells (second punch). Senotherapeutics block secretory expression, a collection of pro-inflammatory cytokines, tissue remodeling proteins, and inflammation. Since tumors are heterogeneous or diverse within cell populations and between tumors, examining the genetic and molecular profile of the tumor after treatment is key to creating an effective second punch of senotherapeutics. Being able to deliver a treatment that targets the major signaling pathways of the senescent cells in a patient’s particular tumor will create a more profound and overarching impact and eliminate a higher number of senescent cells. These second-punch treatments may need to be repeated over the course of months or years because senescent cells sometimes become reactivated and signal to their neighbors to become damaged again or proliferate, leading to tumor recurrence. This one-two-punch treatment, however, is only beneficial for cancer therapies, and further research will need to be completed on targeting other diseases, such as neurodegenerative or mobility and eyesight diseases.

We can also harness the use of senotherapeutics for aging or age-related diseases. Since unresolved clearance of senescent cells and their secretory phenotypes can result in changes to the tissues and organs characteristic of aging, being able to target and eliminate them from specific areas would greatly reduce the risk of disease. One example is in skin aging, where DNA damage from the sun accumulates in cells in the epidermis and dermis of the skin. This can lead to inflammation, fibrotic changes, and fat atrophy causing wrinkle formation and possible melanoma. Senolytics, which selectively kill senescent cells, and senomorphics, which rejuvenate senescent cells, are both treatment types that should be analyzed depending on the therapeutic aim. Senolytics do not have the ability to tell which senescent cell types they are targeting, some of which may be beneficial. Senomorphics may require repeat applications and may retain some features of aging. These therapies are still in pre-clinical trials and need further exploration before developing into human treatments.

Overall, senescent cells exhibit positive and negative impacts, depending on what stage you are in your life. They are positive for reducing tumor growth but negative because they can increase inflammation and are associated with age-related diseases. This research avenue is still in its infancy and has a long way and many trials to go before being marketed to the public. For now, discovering the intricacies of senescent cells and targeting them more completely with senotherapeutics, especially in cancer treatment, would bring scientists a long way in understanding the potential therapeutic use of these cells. ● ● ●

