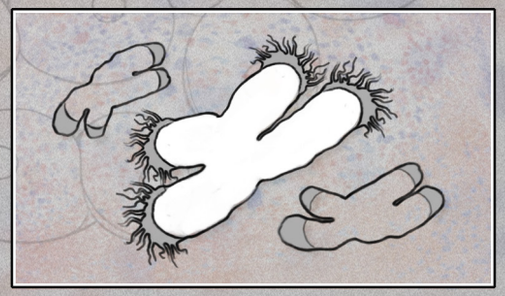
THE INTERPLAY OF CELL SENESCENCE AND AGING

Senescent cells accumulate with age. This may result in higher levels of certain senescence-associated secretory phenotype (SASP) proteins, which researchers believe drive aging-related processes and promote aging-related diseases. And senescence, scientists are coming to understand, is itself mediated by cellular processes associated with aging.

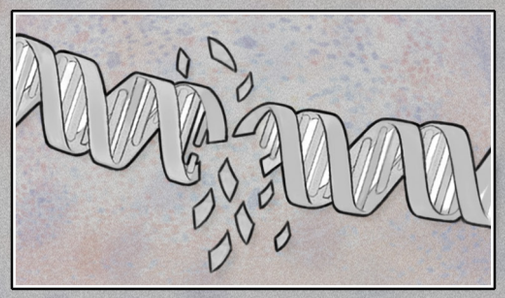
TELOMERE DYSFUNCTION

This can occur when protective pieces of DNA at the ends of chromosomes grow shorter with successive cell divisions, or when their internal structure unfolds, a process called "telomere uncapping." Both have been shown to trigger senescence in vitro.



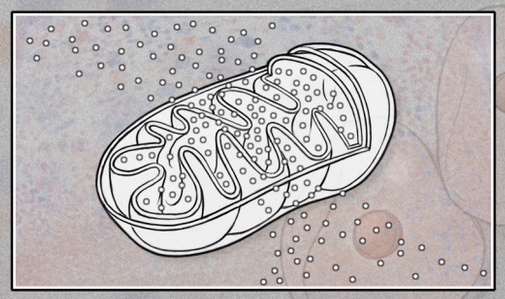
POTENTIALLY ONCOGENIC MUTATIONS

As DNA repair mechanisms erode with age, cells can acquire certain mutations, particularly those that activate oncogenes, that push cells into senescence.



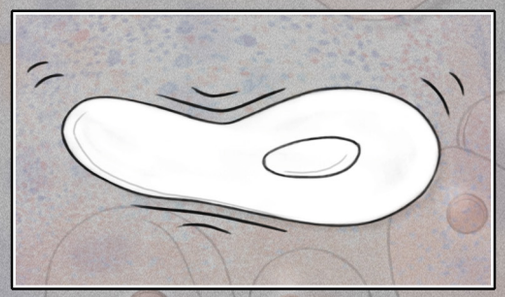
REACTIVE METABOLITES

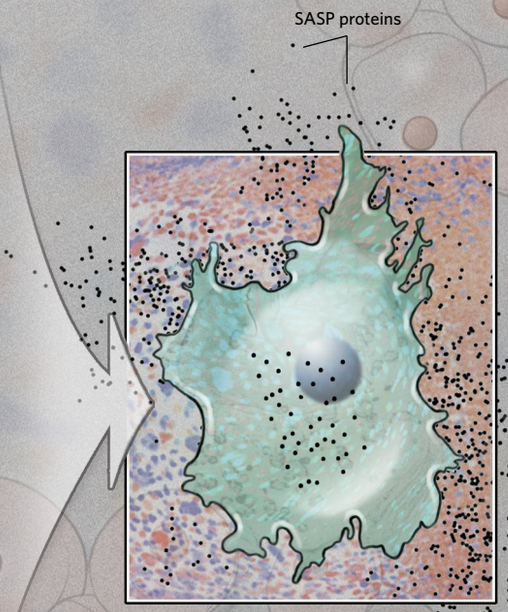
Several cellular organelles, especially mitochondria, can generate reactive oxygen species (ROS) that damage both mitochondrial and nuclear genomes and thereby drive senescence. The production of ROS is thought to increase with age.



OTHER PROCESSES

Several other mechanisms may drive senescence. For example, mechanical stress might lead to senescence of cells in joints, and the epigenetic machinery that governs gene expression is thought to become dysregulated with age, which may somehow induce senescence.





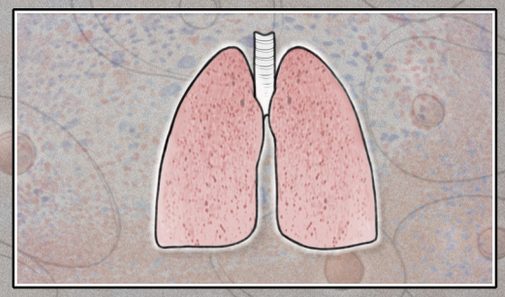
HOW AGING-RELATED CELLULAR PROCESSES DRIVE SENESCENCE:

Untangling which cellular processes drive senescence is a major challenge to researchers, in part because those pathways are interrelated. In addition, there may well be multiple factors that contribute to the accumulation of senescent cells, including the tissue or organ in question, a person's genetic makeup, and environmental stressors she is exposed to.

CATHERINE DELPHIA

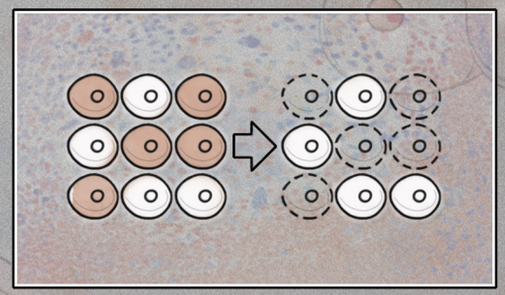
HOW SENESCENCE CAN DRIVE AGING-RELATED PROCESSES:

Chronic inflammation and the exhaustion of stem cells are thought to be the most significant consequences of senescence in aging tissues, although other effects are being explored. The importance of these processes may differ depending on the condition in question.



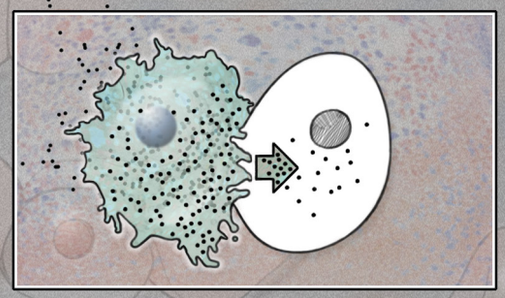
CHRONIC INFLAMMATION

Senescent cells secrete proinflammatory cytokines, which trigger chronic immune reactions that may drive many aging-related diseases.



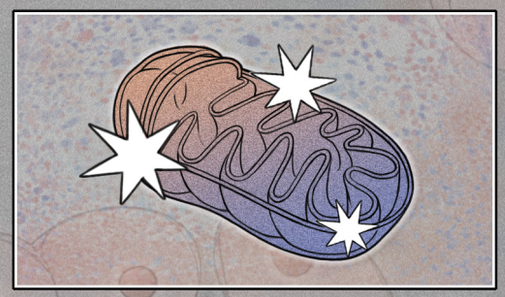
STEM CELL EXHAUSTION

With age, stem cells throughout the body likely undergo senescence, limiting the body's ability to regenerate tissue and ultimately compromising tissue function.



SENESCENCE IN NEIGHBORING CELLS

Senescent cells can prompt other cells around them to undergo senescence through the secretion of particular signaling proteins, a process termed "paracrine senescence."



OTHER PROCESSES.

Some studies suggest that the secretions of senescent cells can induce mitochondrial dysfunction in neighboring cells, generating ROS that drive tissue damage and cell senescence in surrounding tissues. Senescent cells have also been implicated in the formation of misfolded proteins such as tau and amyloid-β, aggregations of which are associated with neurodegenerative disease and have been suggested to drive senescence themselves.