Targetting zombie cells: Potential of senolytics in slowing aging and promoting longevity

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Damaged cells known as senescent cells, are those that stop reproducing but keep being metabolically active, secreting harmful substances and consequently triggering the inflammation and damage of the surrounding cells. They are termed zombie cells because they do not die naturally but still cause harm. The continuous accumulation of such cells is implicated in the process that leads to tissue degeneration, chronic inflammation, as well as the development of many other age-related diseases. One of the creative paths for enhancing the quality and length of life is to use senolytics, a category of medications that specifically eliminate senescent cells. Apoptosis and homeostasis is restored with these drugs that block the survival pathways of such cells.[1]

Preclinical trials have shown that long-term use of these drugs can delay the onset of, or drastically improve a number of, the so-called age-related diseases such as cardiovascular disease, diabetes, osteoarthritis, and neurodegenerative disorders.[1] However, in 2019, the first human trial of senolytic therapy, conducted with the combination of dasatinib and quercetin (D+Q), was done on patients with idiopathic pulmonary fibrosis (IPF), which is an age-related progressive lung disease.[2] The open-label pilot study has reported very positive outcomes, with the treatment being well tolerated and suggestible to the increase in physical function. A later run of a randomized controlled trial also confirmed the safety and practicality of D+Q in IPF besides prolonged and better functional status.[3]

Along with the positive developments, several crucial inquiries are left unanswered. The senolytics may not be fully selective and as a result, they may also affect normal cells, thus impairing tissue repair.[4] Although senescent cells are one of the contributors to the elderly syndromes, they are also the key entities in the processes of wound healing, immune surveillance, and tumor suppression.[1,4,5] Moreover, the ideal dosage, schedule, and duration of senolytic therapy are still not determined.[4]

Although long-term efficacy and safety remain unclear, recent research could enable the creation of safer, more targetted delivery mechanisms. The very high cost of senolytic drugs is an added challenge, raising concerns about access equity. However, continued clinical evaluation and technological refinement promise to unlock transforming senolytics into a successful tool for extending health span and improving quality of life in aging populations.

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