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Perspective

Senolytics in Ageing Factors: A Potential Strategy to Prolong Health Span

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DESCRIPTION

Aging is a universal biological process that affects all living organisms. While it is a natural part of life, it is also associated with a range of physical and cognitive decline, leading to an increased susceptibility to age-related diseases and a reduced quality of life. Over the years, scientists have been striving to unravel the mysteries of aging and find ways to extend health span, the period of life spent in good health. One potential avenue of research in this pursuit is the development of senolytics, compounds that target and eliminate senescent cells, which play a pivotal role in the aging process.

Understanding the aging process

Aging is a complex and multifaceted process influenced by a myriad of genetic, environmental, and lifestyle factors. Several theories have been proposed to explain the mechanisms underlying aging, each shedding light on different aspects of the process.

Senescent cells as key elements in aging

Cellular senescence is a key element in the aging process. Senescent cells accumulate in various tissues and organs throughout the body, contributing to tissue dysfunction and the development of age-related diseases. These cells not only lose their normal functions but also secrete a cocktail of harmful molecules that can negatively impact neighboring cells and tissues.

Senescent cells can arise from different sources, including telomere shortening, DNA damage, and stress signals. When they accumulate, they can disrupt tissue homeostasis and promote inflammation, tissue degradation, and fibrosis. This chronic low-level inflammation can, in turn, contribute to the onset and progression of age-related diseases, such as atherosclerosis, osteoarthritis, and Alzheimer's disease.

The role of senolytics in aging

Senolytics are a class of drugs or compounds designed to target and eliminate senescent cells selectively. The primary goal of senolytics is to clear these dysfunctional cells from tissues, reducing inflammation and preventing the propagation of the Senescence-Associated Secretory Phenotype (SASP). This approach has generated immense interest in the scientific community and is seen as a potential breakthrough in the quest to extend health span and delay the onset of age-related diseases.

Senolytics can be broadly categorized into two classes:

Apoptosis-inducing senolytics: These compounds trigger programmed cell death (apoptosis) specifically in senescent cells. By activating apoptotic pathways in senescent cells, these senolytics facilitate the removal of these dysfunctional cells from tissues.

Senescent cell-targeting agents: Senescent cell-targeting agents are designed to recognize and bind to specific markers on the surface of senescent cells. This binding allows for the selective elimination of senescent cells through the body's natural immune system, such as through phagocytosis by macrophages.

Prominent senolytics

Several senolytic compounds have shown the potential in preclinical and clinical studies. Some of the notable senolytics include:

Dasatinib and quercetin: A combination of the cancer drug dasatinib and the flavonoid quercetin has gained attention as an effective senolytic therapy. It has demonstrated the ability to clear senescent cells and alleviate age-related symptoms in animal models.

Navitoclax (ABT-263): Navitoclax is an inhibitor of Bcl-2, a protein that promotes cell survival. It has shown senolytic properties by inducing apoptosis in senescent cells, particularly in blood stem cells.

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Fisetin: Fisetin is a natural compound found in fruits and vegetables, such as strawberries and apples. It has shown senolytic activity by targeting and eliminating senescent cells.

Clinical applications and challenges

While senolytics show vital potential, there are several challenges to their widespread clinical application:

Selectivity: Ensuring that senolytics specifically target senescent cells while sparing healthy cells is vital to minimize potential side effects.

Timing: Determining the optimal timing for senolytic interventions is complex. It is essential to strike a balance between eliminating harmful senescent cells and preserving functional ones.

Safety: The long-term safety of senolytic treatments needs further investigation, especially given that senescent cells play some beneficial roles, such as in wound healing and cancer prevention.

CONCLUSION

Aging is a complex biological process influenced by a multitude of factors, including cellular senescence, telomere shortening, mitochondrial dysfunction, and genetic/epigenetic factors. Senescent cells, in particular, play a pivotal role in aging, as they accumulate with age and contribute to tissue dysfunction and inflammation.

Senolytics offer an effective approach to combat aging factors by selectively targeting and eliminating senescent cells. These compounds have shown potential in preclinical and clinical studies, with the goal of extending health span and delaying the onset of age-related diseases. However, several challenges, including selectivity, timing, safety, combination therapies, and regulatory approval, must be addressed before senolytics can become widely available anti-aging interventions.