

Targeting Autophagic Dysfunction to Mitigate Cellular Senescence in Age-Related Diseases: An Innovative Approach

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Abstract. Cellular senescence plays a pivotal role in aging and the pathogenesis of age-related diseases, posing a significant challenge for therapeutic intervention. This study investigates the interplay between autophagy and senescence, exploring how modulating autophagic pathways can alleviate the detrimental effects of senescent cells. We employed a combination of biochemical assays, cellular models, and innovative imaging techniques to assess the effectiveness of autophagy inducers in rejuvenating senescent phenotypes. Our findings demonstrate that enhancing autophagic activity can restore cellular function and reduce senescence-associated secretory phenotype (SASP) factors, presenting a viable therapeutic target for managing age-related conditions. This research underscores the importance of autophagy in cellular homeostasis and its potential in combating the aging process. We suggest future research directions focused on translating these findings into clinical applications.

Keywords: cellular senescence, autophagy, aging, age-related diseases, SASP, therapeutic intervention, cellular homeostasis, regenerative capacity, inflammation

Introduction

Cellular senescence, characterized by permanent cell cycle arrest, is increasingly recognized as a critical contributor to the aging process and various age-related diseases such as cancer, cardiovascular diseases, and neurodegenerative disorders. As the global population ages, the incidence of these diseases rises, underscoring the urgency for innovative therapeutic strategies. Cellular senescence is induced by various stressors, including telomere shortening, DNA damage, and oxidative stress, leading to a senescence-associated secretory phenotype (SASP) that exacerbates tissue dysfunction and inflammation. Notably, the accumulation of senescent cells has been linked to the decline

in regenerative capacity and the onset of frailty in the elderly, making it a focal point for research aimed at extending healthspan. Recent studies have highlighted the role of autophagy, a cellular degradation process crucial for maintaining cellular homeostasis, in regulating senescence. Deficient autophagic activity has been observed in senescent cells, suggesting that restoring autophagy could mitigate the negative consequences of cellular aging. This paper aims to elucidate the relationship between autophagy and cellular senescence, proposing that targeted modulation of autophagic pathways can serve as a novel therapeutic approach to counteract age-related diseases. The structure of this paper is as follows: we will first delve into the mechanisms of cellular senescence and its implications for aging, followed by a discussion on the role of autophagy in cellular function. Subsequently, we will present our experimental findings on autophagic modulation and its effects on senescent cells, culminating in a discussion on the translational potential of these insights for therapeutic intervention.

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