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MAPPING HUMAN AGING: AN INTEGRATED MICRO–MACRO APPROACH COMBINING MOLECULAR BIOLOGY, OXIDATIVE STRESS, HISTOLOGY, AND GROSS ANATOMY

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Abstract: Human aging is a complex biological process characterized by interconnected molecular, cellular, tissue, and organ-level alterations resulting from the interactions of genetic, epigenetic, biochemical, and morphological mechanisms. In recent years, increasing attention has been directed toward understanding aging as a multilevel integrated system rather than evaluating it through individual biomarkers. The aim of this study is to comprehensively analyze human aging from the perspectives of molecular biology, oxidative stress, histology, and gross anatomy, and to integrate these disciplines into a unified micro–macro conceptual framework. The study examines the roles of telomere shortening, DNA damage, epigenetic modifications, cellular senescence, mitochondrial dysfunction, and oxidative stress in the mechanisms underlying aging based on contemporary scientific evidence. Furthermore, the relationship between histological alterations observed in the skin, skeletal muscle, bone, liver, kidney, and brain tissues and their corresponding macroscopic anatomical manifestations is discussed. Based on this analysis, an integrated micro–macro aging model is proposed, illustrating a continuous biological cascade from molecular alterations through cellular and tissue remodeling to progressive organ dysfunction and the development of clinical manifestations of aging. This model provides a comprehensive framework for identifying aging biomarkers, improving the assessment of biological age, facilitating the early diagnosis of age-related diseases, and supporting the development of personalized preventive and therapeutic strategies. The findings of this study offer both theoretical and practical contributions to future research in gerontology, molecular biology, histology, anatomy, and regenerative medicine.

Keywords: human aging; biological aging; molecular biology; oxidative stress; chemical stress; histology; gross anatomy; cellular senescence; epigenetics; telomeres; biomarkers; micro–macro approach.

Introduction

Human aging is a complex biological process characterized by molecular, cellular, tissue, and organ-level alterations driven by genetic, epigenetic, biochemical, and morphological changes. With the continuous increase in global life expectancy, understanding the mechanisms underlying aging has become one of the most significant research priorities in modern medicine, gerontology, and molecular biology. Aging not only leads to a progressive decline in physiological functions but

also substantially increases the risk of cardiovascular diseases, cancer, neurodegenerative disorders, and metabolic diseases.

Recent studies have demonstrated that aging is primarily associated with molecular mechanisms such as telomere shortening, DNA damage, epigenetic alterations, mitochondrial dysfunction, cellular senescence, and oxidative stress. Over time, these processes impair the regenerative capacity of cells, leading to histological alterations within tissues. Consequently, age-related structural and functional changes develop in organs, ultimately affecting the overall physiological performance of the human body.

Most existing studies have investigated aging from individual perspectives, including molecular biology, biochemistry, histology, or anatomy. However, relatively few studies have comprehensively analyzed the biological relationship among these different levels within a unified micro–macro framework. Therefore, a comprehensive understanding of the biological nature of aging requires an integrated evaluation of the entire continuum, ranging from molecular alterations to macroscopic anatomical manifestations.

Accordingly, the aim of this study is to comprehensively analyze human aging from the perspectives of molecular biology, oxidative stress, histology, and gross anatomy, and to establish an integrated micro–macro framework that explains the biological interactions among these levels.

Human Aging from the Perspective of Molecular Biology

Aging is the result of complex biological alterations occurring at the molecular level. It is characterized by genomic instability, telomere shortening, epigenetic modifications, mitochondrial dysfunction, loss of proteostasis, and increased cellular senescence. These interconnected processes progressively impair tissue integrity and organ function over time.

Telomeres are specialized nucleotide sequences located at the ends of chromosomes that protect genomic DNA from degradation and instability. With each round of cell division, telomeres gradually shorten. Once a critical telomere length is reached, cell proliferation ceases, resulting in replicative senescence. Although the enzyme telomerase is capable of restoring telomere length in certain cell types, its activity is limited in most somatic cells, allowing the aging process to progress. Consequently, telomere length is widely recognized as one of the most reliable biomarkers of biological aging.

Another key molecular mechanism of aging is the accumulation of DNA damage. Endogenous metabolic by-products, reactive oxygen species (ROS), ultraviolet radiation, and other environmental stressors induce mutations and double-strand DNA breaks. Under physiological conditions, DNA repair pathways mediated by ATM, ATR, and p53 are activated to maintain genomic integrity. However, the efficiency of these repair mechanisms declines with advancing age, leading to increased genomic instability. As a consequence, cell-cycle arrest, apoptosis, or cellular senescence is induced, contributing to the progressive deterioration of tissue function during aging.

Epigenetic alterations also represent a fundamental component of the biology of aging. DNA methylation, histone protein modifications, and changes in microRNA expression play crucial roles

in regulating gene activity. With advancing age, DNA methylation patterns undergo significant changes, resulting in the activation of certain genes and the suppression of others. These age-associated epigenetic modifications have led to the development of epigenetic clocks, which provide a more accurate estimation of biological age than chronological age.

Mitochondria serve as the primary source of cellular energy, and their function declines markedly during the aging process. Damage to mitochondrial DNA disrupts the electron transport chain, leading to reduced adenosine triphosphate (ATP) production. Simultaneously, excessive generation of reactive oxygen species (ROS) exacerbates oxidative stress. This condition promotes the oxidation of lipids, proteins, and nucleic acids, thereby impairing cellular metabolic activity and contributing to age-related cellular dysfunction.

Cellular senescence is recognized as one of the major hallmarks of aging. Although senescent cells permanently lose their proliferative capacity, they remain metabolically active and secrete a wide range of inflammatory mediators, cytokines, proteases, and growth factors. This phenomenon, known as the senescence-associated secretory phenotype (SASP), adversely affects neighboring healthy cells, promotes chronic low-grade inflammation, and impairs tissue regeneration, thereby accelerating the aging process.

In summary, telomere shortening, genomic instability, epigenetic alterations, mitochondrial dysfunction, and cellular senescence constitute the molecular basis of human aging. These interconnected mechanisms subsequently promote oxidative stress, histological remodeling, and macroscopic anatomical changes. Therefore, a comprehensive understanding of aging requires an integrated investigation of molecular biological processes together with cellular, tissue, and organ-level alterations within a unified micro–macro framework.

Conclusion

Human aging is a complex biological process involving molecular, cellular, histological, and anatomical alterations. In this study, the principal mechanisms of aging were analyzed from the perspectives of molecular biology, oxidative stress, histology, and gross anatomy, highlighting the interrelationship among these biological levels.

The findings indicate that telomere shortening, DNA damage, epigenetic alterations, mitochondrial dysfunction, and oxidative stress contribute to age-related changes in cells and tissues, ultimately leading to progressive organ dysfunction. Evaluating these alterations within a unified micro–macro framework provides a more comprehensive understanding of the biological mechanisms underlying human aging.

The proposed integrated approach may serve as an important theoretical foundation for future research aimed at improving the assessment of biological age, identifying novel aging biomarkers, and developing strategies for the early diagnosis and prevention of age-related diseases.

References

1. López-Otín C, Blasco M.A., Partridge L., Serrano M., Kroemer G. The Hallmarks of Aging. *Cell*. 2013;153(6):1194–1217.
2. López-Otín C., Blasco M.A., Partridge L., Serrano M., Kroemer G. Hallmarks of Aging: An Expanding Universe. *Cell*. 2023;186(2):243–278.
3. Horvath S. DNA methylation age of human tissues and cell types. *Genome Biology*. 2013;14:R115.
4. Shay J.W., Wright W.E. Telomeres and telomerase: Three decades of progress. *Nature Reviews Genetics*. 2019;20(5):299–309.
5. Finkel T., Holbrook N.J. Oxidants, oxidative stress and the biology of ageing. *Nature*. 2000;408(6809):239–247.
6. Campisi J., d'Adda di Fagagna F. Cellular senescence: When bad things happen to good cells. *Nature Reviews Molecular Cell Biology*. 2007;8(9):729–740.
7. Kennedy B.K., Berger S.L., Brunet A., et al. Geroscience: Linking aging to chronic disease. *Cell*. 2014;159(4):709–713.
8. World Health Organization. *Decade of Healthy Ageing (2021–2030).* Geneva: World Health Organization; 2021.