

Review Article

Environmental Influences on Genetic Aging Processes: Experimental Evidence from Model Systems

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Abstract

Aging is a complex biological process influenced not only by genetic predispositions but also significantly shaped by environmental factors. This review synthesizes experimental evidence from model systems elucidating how environmental exposures modulate genetic aging processes. Studies in organisms such as *Caenorhabditis elegans*, mice, and human cellular models demonstrate that external conditions including diet, psychosocial stress, pollutants, and physical activity interact dynamically with genetic and epigenetic regulators to influence lifespan and healthspan. Advances in molecular biology and omics technologies reveal mechanisms such as DNA methylation alterations, histone modifications, telomere attrition, oxidative stress, and cellular senescence as critical mediators of gene-environment crosstalk in aging. Genetic manipulation tools like CRISPR and RNA interference enable precise interrogation of genes implicated in environmental responses, deepening understanding of aging pathways. While model organisms provide invaluable platforms to dissect these interactions, challenges remain in translating findings to human aging due to complexity and heterogeneity. Future directions highlight emerging single-cell multiomics, organ-on-chip systems, and artificial intelligence integration to unravel aging's multifactorial nature. The review underscores the necessity of multidisciplinary approaches combining genetics, environmental sciences, and computational biology to develop therapeutic strategies aimed at modulating environmental factors to promote healthy aging. These insights pave the way for personalized interventions targeting both genetic susceptibilities and modifiable environmental risks, ultimately advancing longevity and well-being.

Keywords

Epigenetic Modifications, Model Organisms, Aging Biomarkers, Genetic Manipulation, Environmental Exposures

1. Introduction

Aging is a multifactorial biological process characterized by progressive functional decline, intricately regulated by the dynamic interplay of genetic and environmental factors [1, 2]. Genetic predispositions establish the foundational blueprint influencing lifespan and vulnerability to age-related diseases, yet environmental exposures ranging from lifestyle choices to broader social determinants, significantly modulate individual

aging trajectories [2]. Comprehensive recent studies, such as those leveraging the UK Biobank data, reveal that environmental factors collectively account for a substantially larger portion of variability in aging outcomes and mortality than genetics alone, underscoring the pivotal role of the exposome, which represents the sum of all lifetime environmental exposures [3].

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This exposome encompasses a multitude of factors including socioeconomic status, smoking, physical activity, mental wellness, and early life conditions, which interact additively to influence proteomic aging signatures, disease risk, and life expectancy [3]. While genetic risk scores explain a notable proportion of variation for specific age-related diseases like certain cancers and dementias, environmental drivers predominantly shape the overall aging landscape and premature mortality patterns. These findings highlight the necessity to integrate environmental context alongside genetic considerations to fully understand the aging process and develop targeted interventions for healthy aging [3].

Understanding how environmental factors modulate genetic aging processes is crucial to reveal the molecular mechanisms and pathways by which external stimuli contribute to genomic instability, epigenetic changes, and gene-environment interactions that drive aging and related diseases [4]. Environmental exposures profoundly impact the aging phenotype by inducing DNA damage, altering epigenetic regulation, influencing telomere dynamics, and reshaping cellular homeostasis, thereby accelerating or decelerating aging trajectories [3, 5].

Experimental model organisms such as yeast, worms, flies, and mice have been essential for dissecting these complex mechanisms, offering controlled systems to study how environment shapes genetic pathways that regulate lifespan and healthspan [6]. For example, UV radiation, dietary factors, pollutants, and psychosocial stress have been shown to impact genetic and epigenetic markers of aging in these models [7]. Through these studies, potential intervention points emerge to mitigate environmental damage and promote healthy aging.

This review aims to synthesize experimental evidence from diverse model systems to elucidate how environmental factors influence genetic aging processes. The focus includes studies on genetic instability, epigenetic modifications, telomere dynamics, gene-environment interactions, and the exposome framework. By integrating these findings, the review delineates the mechanistic pathways through which environment shapes genetic aging and highlights future directions to deepen our understanding of aging biology in the context of environmental influences.

2. Genetic Basis of Aging

Aging is regulated by key genetic pathways that govern cellular function and longevity, including telomere attrition, cellular senescence, and DNA repair mechanisms [1, 8, 9]. Telomeres, which cap chromosome ends, progressively shorten with each cell division, eventually triggering senescence or apoptosis when critically shortened [8]. Cellular senescence serves as a permanent cell cycle arrest state induced by various stresses, including DNA damage and telomere dysfunction, contributing to tissue aging. Efficient DNA repair pathways maintain genomic stability, and their decline accelerates aging and predisposes to age-related diseases [10].

Experimental model organisms such as *Caenorhabditis elegans*, *Drosophila melanogaster*, and mice are widely used to dissect these genetic aging pathways due to their genetic tractability and conserved mechanisms across species [11]. Genetic markers of aging and longevity include telomere length, expression of senescence-related genes like p16 INK4a, and genetic variants affecting DNA repair and metabolic functions. These markers, along with epigenetic signatures, provide valuable insights into individual aging processes and potential targets for intervention to promote healthy aging [12, 13].

3. Environmental Factors Impacting Genetic Aging

Environmental factors represent a diverse set of physical, chemical, biological, and lifestyle exposures that exert significant influence on genetic aging processes [3, 4]. These factors modulate aging by inducing molecular damage, altering gene expression, and affecting cellular homeostasis, thereby accelerating or decelerating biological aging [14].



Figure 1. Environmental factors Impacting genetic aging.

3.1. Physical Environmental Influences

Environmental temperature is a key physical factor influencing genetic aging, with its effects extensively studied in model organisms. Generally, higher temperatures tend to accelerate the aging process and reduce lifespan, as observed in *Caenorhabditis elegans* where warm temperatures induce neuronal control mechanisms that regulate longevity-associated gene expression, including genes implicated in stress resistance and proteostasis [15]. Conversely, cooler

environments have been shown to extend lifespan and delay age-related decline by modulating metabolic and gene expression networks [16]. These temperature-dependent changes underscore the adaptability of genetic pathways to environmental cues, impacting aging through conserved molecular mechanisms [15].

Radiation exposure, particularly ultraviolet (UV) and ionizing radiation, represents another critical physical environmental influence on genetic aging [17]. UV radiation induces specific DNA lesions, such as cyclobutane pyrimidine dimers, which compromise genomic integrity and activate DNA damage response pathways [18]. Ionizing radiation causes double-strand breaks, triggering complex repair processes; failure or inefficiency in these pathways accelerates genetic instability and promotes cellular senescence. Persistent DNA damage from radiation exposure is linked to tissue degeneration and increased risk of age-related diseases, highlighting the importance of DNA repair mechanisms in mitigating environmentally induced genetic aging [17].

Mechanical stress also impacts cellular aging by modulating the physical forces experienced by cells within tissues [19]. This stress affects cytoskeletal integrity, mechanotransduction signaling, and extracellular matrix remodeling, which collectively influence cellular function and senescence. Chronic mechanical stress can lead to alterations in gene expression related to inflammation and matrix degradation, contributing to functional decline in aged tissues [1]. Together, temperature variations, radiation, and mechanical forces illustrate the diverse physical environmental factors that interact with genetic mechanisms to shape aging trajectories.

3.2. Chemical Environmental Influences

Chemical environmental factors such as toxins and pollutants significantly impact genetic stability and aging processes. Exposure to heavy metals, pesticides, and air pollutants induces oxidative stress and DNA damage, thereby accelerating genomic instability and cellular senescence [20]. These toxicants disrupt cellular homeostasis through reactive oxygen species (ROS) generation, impairing DNA repair pathways and triggering inflammatory responses associated with aging. In contrast, dietary compounds and caloric restriction exert profound effects on aging pathways [21]. Caloric restriction, defined as reduced calorie intake without malnutrition, consistently extends lifespan and health span across diverse model organisms by modulating key metabolic and stress response pathways [22]. This includes downregulation of insulin/IGF-1 and Target of Rapamycin (TOR) signaling, activation of AMP-activated protein kinase (AMPK), and sirtuin proteins, collectively enhancing mitochondrial function, antioxidant defenses, and autophagy [23]. The hormesis effect of caloric restriction induces protective stress responses mitigating oxidative damage, thus delaying aging progression. Moreover, antioxidants from diet play a crucial role in neutralizing ROS, bolstering endogenous defenses against oxi-

dative stress, a major driver of aging and age-related diseases [24]. Together, the interplay of harmful chemical exposures and beneficial dietary factors shapes the genetic and molecular landscape of aging [24].

3.3. Biological Environmental Influences

The composition of the host microbiome plays a pivotal role in modulating aging-related genetic processes [25]. Age-associated shifts in gut microbiota are characterized by reduced microbial diversity and an increase in opportunistic pathogens, which disrupt immune homeostasis and exacerbate chronic inflammation, a key driver of aging and cellular senescence. Dysbiosis influences host gene expression by altering metabolic pathways and immune signaling, thereby impacting DNA repair and genome stability [26]. Beneficial microbial metabolites, such as short-chain fatty acids, have been shown to support DNA repair mechanisms and temper inflammatory responses, highlighting the gut microbiome as a regulator of genetic aging [27]. Pathogen exposure further contributes to immune system aging or immunosenescence by provoking chronic immune activation and exhaustion, which impair immunological resilience and increase susceptibility to age-related diseases [28]. Additionally, environmental endocrine disruptors interfere with hormonal signaling pathways, disrupting endocrine homeostasis and accelerating aging through epigenetic modifications and altered gene regulation. Together, these biological environmental influences intricately interact with the genetic framework of aging, presenting avenues for therapeutic modulation of aging processes [29].

3.4. Lifestyle and Behavioral Environmental Factors

Physical activity exerts profound anti-aging effects at the genetic and cellular levels. Exercise minimizes genomic instability, a hallmark of aging, by reducing DNA damage and enhancing repair mechanisms along with resistance to oxidative stress [30]. It also counters telomere attrition by increasing telomerase activity and upregulating proteins that preserve telomere length, which is directly linked to longevity and muscle regeneration in older adults [31]. Furthermore, physical activity induces widespread epigenetic modifications, including DNA methylation changes, histone modifications, and miRNA expression in tissues such as muscle and brain. These changes affect gene expression patterns important for maintaining cellular health during aging [32]. Exercise also promotes proteostasis by regulating autophagy pathways and mitochondrial function, combating the mitochondrial dysfunction typical of aging cells. Regular exercise increases mitochondrial biogenesis and oxidative capacity, which helps sustain muscle function and systemic health. Through these mechanisms, physical activity can delay typical age-related physical decline, reprogram aging genes epigenetically, and contribute to healthier lifespan extension [33].

Psychological stress has significant epigenetic effects that influence biological aging. Stress induces changes in DNA methylation and other epigenetic modifications that regulate gene expression related to aging pathways [32]. Chronic stress can accelerate epigenetic aging, leading to earlier onset of age-related diseases and functional decline. These epigenetic alterations may be mediated via changes in inflammation, oxidative stress, and hormonal signaling pathways [34]. Notably, some stress-induced epigenetic marks can be transmitted across generations, potentially affecting the health and aging trajectories of offspring. Thus, psychological stress acts as an environmental factor modulating the epigenome in ways that contribute to accelerated biological aging and increased vulnerability to disease [32].

Sleep patterns and circadian rhythms play critical roles in regulating aging genes. Aging disrupts circadian rhythmicity, causing a phase shift toward morning chronotypes and loss of robust oscillations in core clock genes and over a thousand other genes regulating physiological processes such as cognition, mood, and metabolism [35]. This disruption in circadian gene expression contributes to sleep disturbances, mood disorders, and cognitive decline frequently observed in older adults [36]. Conversely, some genes gain rhythmicity with age, possibly as a compensatory mechanism to counterbalance circadian dysfunction. Proper sleep and circadian regulation are therefore essential to maintain the rhythmic control of aging-related genes, and disruptions in these systems accelerate the aging process at the molecular and systemic levels [37].

4. Experimental Evidence from Model Systems

Experimental studies in model systems have significantly advanced our understanding of environmental-genetic interactions in aging [38]. Large-scale analyses, such as those using data from model organisms including *Caenorhabditis elegans*, yeast, and mice, demonstrate how environmental inputs like diet, stress, and physical activity interface with genetic and epigenetic factors to modulate lifespan and healthspan [39]. For example, in *C. elegans*, transcriptomic approaches have revealed how gene expression variance across isogenic populations provides insight into physiological heterogeneity in aging. Computational models developed from such data describe fundamental aging processes, including the accumulation and clearance rates of senescent cells and stochastic events triggering aging trajectories at the cellular level [40]. These models successfully recapitulate observed mortality patterns and lifespan differences in mutant and wild-type populations, showing the combined effect of genetic predispositions and environmental triggers [41].

At the molecular and cellular levels, key mechanisms uncovered include epigenetic modifications such as DNA methylation and histone modifications that respond dynamically to environmental changes, influencing gene expression

programs regulating aging [42]. The role of reactive oxygen species (ROS), mitochondrial function, proteostasis, DNA repair capacity, and inflammation signaling are widely studied mechanisms modulated by both genetic factors and external stimuli [43]. Senescent cell accumulation, mitochondrial dysfunction, and stochastic DNA damage emerge as critical nodes where environment intersects with genetic aging pathways. These mechanisms are also influenced by systemic factors such as hormonal changes and circadian regulation, further integrating environmental inputs into aging biology [42].

Gene-environment interaction models of aging emphasize the epigenetic landscape as a crucial mediator [4]. Environmental exposures induce heritable epigenetic modifications that can either accelerate or decelerate cellular aging. Studies using proteomic and transcriptomic clocks have mapped how exposures to stress, toxins, diet, and exercise translate into molecular changes that shift biological age independent of chronological age [44]. This interaction creates complex feedback loops where genetics modulate environmental sensitivity and environmental factors alter gene expression through epigenetic remodeling. Collectively, these models underscore aging as a plastic process shaped by the dynamic interplay between inherent genetic architecture and lifetime environmental experience, mediated largely by epigenetic regulation [45].

5. Methodologies and Tools Used in Experimental Studies

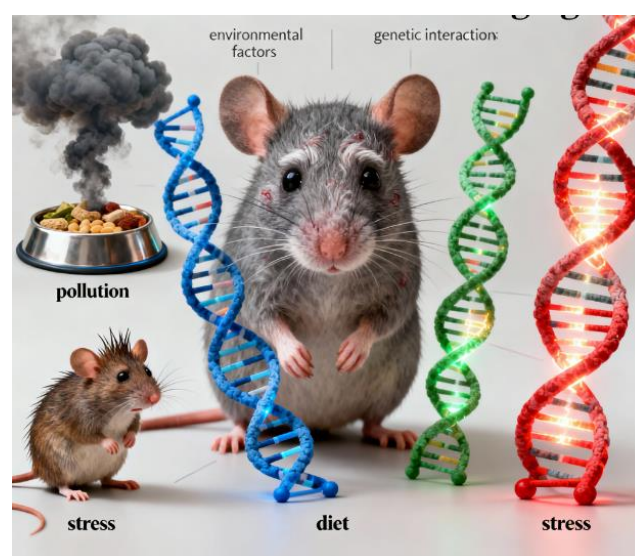


Figure 2. Experimental studies on environmental-genetic interactions in aging.

Experimental studies on environmental-genetic interactions in aging employ a broad array of methodologies and tools, primarily leveraging model organisms and advanced

molecular techniques [46]. Advanced technology has been applied to aging research to investigate genes involved in processes like Genetic manipulation techniques, Omics technologies, Environmental exposure simulations in models, Biomarkers and assays for aging measurement, allowing targeted interventions to mitigate aging-related dysfunction and diseases [47, 48].

5.1. Genetic Manipulation Techniques

Genetic manipulation techniques such as CRISPR/Cas9 and RNA interference (RNAi) have become foundational tools in aging research. CRISPR/Cas9 enables precise and permanent gene editing by targeting specific DNA sequences with guide RNAs, allowing researchers to knockout or modify genes involved in aging processes [49]. For instance, CRISPR has been effectively used to target the LMNA gene in mouse models of Hutchinson Gilford progeria syndrome, reducing production of the toxic progerin protein that accelerates aging symptoms [50]. Additionally, genome-wide CRISPR knockout screens have identified novel senescence-promoting genes, expanding therapeutic possibilities for age-related diseases. This gene-editing system allows multiplexing and works directly in cell lines or animal models without introducing extraneous genetic material, facilitating robust functional studies [51].

RNAi complements CRISPR by enabling transient gene silencing through degradation of target mRNAs. RNAi is widely used for rapid knockdown of gene expression to assess gene function in aging-related cellular pathways [52]. While RNAi results in temporary gene silencing (knock-down), CRISPR provides permanent gene disruption (knock-out). Both approaches are invaluable for dissection of molecular aging pathways, including that regulating senescence, DNA repair, and inflammation [53]. Importantly, these tools facilitate the development of disease models, such as Alzheimer's disease, by introducing or silencing causative mutations to study functional outcomes in relevant cell or animal systems [54]. Together, CRISPR and RNAi accelerate genetic discovery and therapeutic strategy development in aging biology.

5.2. Omics Technologies

Omics technologies have become essential tools in aging research for comprehensively characterizing molecular changes associated with aging at various levels [55]. Transcriptomics involves sequencing and analyzing the global RNA expression patterns in cells or tissues, providing insights into how gene expression alters with age. Studies across multiple model organisms and humans consistently show age-associated downregulation of genes involved in mitochondrial function, protein synthesis, and growth signaling, along with upregulation of genes related to inflammation and DNA damage response [56]. Transcriptomic profiles carry latent information about biological age, enabling the devel-

opment of molecular clocks that predict aging and assess intervention efficacy [55]. Importantly, tissue-specific aging signatures have been identified; for example, brain aging shows distinct transcriptome changes linked to neurodegeneration that can be modulated by lifestyle factors like physical activity [57].

Epigenomics focuses on heritable modifications that regulate gene activity without altering the DNA sequence, such as DNA methylation and histone modifications. Age-related changes in DNA methylation patterns form the basis of epigenetic clocks, some of the most accurate molecular biomarkers of biological aging [55]. Epigenomic profiling reveals how environmental factors influence these modifications to accelerate or decelerate aging processes through gene regulation. Proteomics complements these by quantifying age-related changes in protein abundance, post-translational modifications, and interactions that underlie cellular function decline [57]. By integrating transcriptomic, epigenomic, and proteomic data, researchers gain a multi-layered understanding of aging mechanisms, gene-environment interactions, and potential therapeutic targets [56].

Together, omics technologies enable detailed mapping of molecular aging landscapes, identification of biomarkers for biological age, and mechanistic insights into how genetics and environment converge to influence aging trajectories [58]. These approaches continue to drive progress in personalized aging research and development of anti-aging interventions. Omics technologies play a crucial role in aging research, offering comprehensive insights into molecular changes across different biological layers [59]. Transcriptomics involves analyzing global RNA expression profiles to reveal age-associated gene expression changes. Studies show consistent downregulation of genes related to mitochondrial function, protein synthesis, and growth signaling with aging, alongside upregulation of genes linked to inflammation and DNA damage response [55, 59]. Transcriptomic data can also serve as molecular clocks to predict biological age and assess interventions, with tissue-specific aging signatures highlighted, such as brain aging patterns affected by physical activity [60].

Epigenomics examines heritable chemical modifications like DNA methylation and histone modifications that regulate gene activity without altering DNA sequence. Changes in DNA methylation patterns have led to the development of epigenetic clocks, powerful biomarkers for biological aging [60]. These epigenetic marks dynamically respond to environmental factors, influencing gene regulation and aging rates. Proteomics complements this by quantifying protein abundance and modifications, shedding light on cellular functional decline during aging [61].

5.3. Environmental Exposure Simulations in Models

Environmental exposure simulations in aging research

models involve replicating real-world stressors and conditions to study their impact on biological aging processes [62]. These simulations utilize animal, human, and in vitro systems to mimic chronic psychological stress, oxidative stress, toxin exposure, dietary restriction, physical activity, and pollution [20]. For example, chronic psychosocial stress models activate neuroendocrine pathways like the sympathetic nervous system and hypothalamic-pituitary-adrenal axis, increasing stress hormones that induce cellular damage via reactive oxygen species, DNA damage, telomere shortening, and inflammation, thereby accelerating aging [62]. These controlled exposures allow researchers to dissect molecular pathways linking environmental stressors to classical hallmarks of aging such as mitochondrial dysfunction, cellular senescence, and inflammatory responses [20].

The exposome framework integrates lifelong cumulative environmental exposures including lifestyle, diet, social determinants, and pollutants and their biological consequences on aging [63]. Recent approaches combine high-resolution mass spectrometry, epigenetic profiling, microbiome analysis, and phenotyping to characterize complex mixtures of environmental factors influencing aging biology [3]. Such integrative simulations and omics assessments illuminate how combined environmental and social stressors modulate aging trajectories, contributing to health disparities in diverse populations. Moreover, simulations of environmental disasters like wildfire smoke inhalation demonstrate acceleration of neurological aging, vascular dysfunction, and neuroinflammation, emphasizing the importance of environmental factors in age-related disease etiology [20].

5.4. Biomarkers and Assays for Aging Measurement

Biomarkers and assays for aging measurement are critical for estimating biological age, which reflects an individual's physiological and functional state better than chronological age [64]. Common biomarkers include molecular, cellular, and physiological indicators that change predictably with aging. Molecular biomarkers involve telomere length, where telomeres progressively shorten with cell divisions, signaling cellular aging and risk for age-related diseases [12]. Epigenetic clocks based on DNA methylation patterns at specific CpG sites are among the most accurate and widely used molecular measures of biological age, capable of predicting lifespan and disease risk [65]. These clocks capture dynamic epigenomic changes associated with environmental exposures and lifestyle factors [66].

Other important biomarkers include circulating blood markers like inflammatory cytokines, metabolic profiles, and proteins linked to system functions such as cardiovascular, liver, and kidney health. Recent advances have led to machine learning models using panels of blood biomarkers to predict biological age and mortality risk with high accuracy [64]. Cellular assays such as senescence-associated

β -galactosidase staining identify senescent cells, while assays of mitochondrial function, proteostasis, and reactive oxygen species provide functional measures of aging at the cellular level [12]. Physiological tests in animal models and humans assess muscle strength, cognitive function, and metabolic health as proxy aging measures. Together, these biomarkers and assays form a multi-dimensional toolkit for aging research, intervention evaluation, and personalized health monitoring [67].

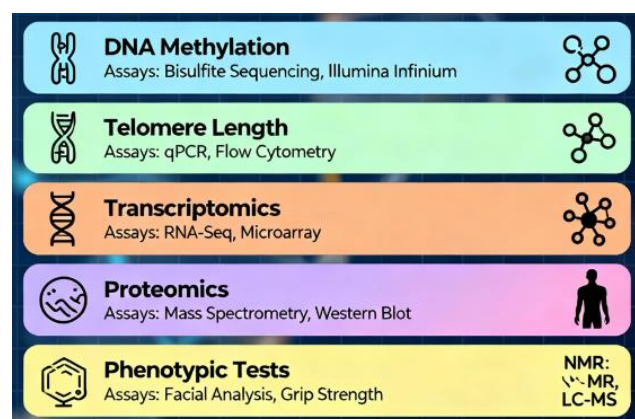


Figure 3. Biomarkers and assays for aging measurement.

6. Challenges and Limitations

Disentangling genetic and environmental factors in aging research is inherently complex due to their intertwined and dynamic nature [3, 4]. Genetics contribute to an individual's baseline susceptibility to aging and age-related diseases, but environmental exposures, lifestyle, and social determinants heavily modulate aging trajectories [68]. For example, environmental pollutants like arsenic and cadmium cause both genetic and epigenetic alterations that accelerate biological aging, and genetic mutations can modify an individual's vulnerability to these toxicants by altering detoxification pathways. Furthermore, biological susceptibility varies across life stages, with early-life exposures imprinting lasting epigenetic changes that influence aging and disease risk later in life, complicating causal analyses [69].

Model system limitations also challenge translation to human aging. While organisms like *C. elegans* and mice provide insights into conserved aging pathways, human aging involves higher complexity and heterogeneity at genetic, physiological, and environmental levels [70, 71]. Many model studies focus on single-factor interventions, whereas humans experience multifactorial, interacting exposures across decades. Differences in lifespan, metabolism, immune systems, and organ function between models and humans complicate extrapolation [70]. Moreover, ethical and technical constraints limit the ability to replicate the full spectrum of human environmental exposures and genetic diversity in experimental settings.

Experimental design in environmental aging research encounters challenges such as controlling for confounding variables, accurately simulating complex, chronic exposures, and measuring subtle phenotypic aging changes over long periods [20]. Longitudinal human cohort studies require extensive resources and participant retention, while animal studies often rely on acute or simplified exposure models. There are also difficulties in integrating multi-omics data to unravel gene-environment interactions due to high dimensionality and variability [72]. Standardized biomarkers and rigor in environmental exposure assessment are critical yet often lacking, hindering reproducibility and cross-study comparison. Addressing these issues is key to advancing mechanistic understanding and developing effective interventions against environmentally influenced aging [3].

7. Future Perspectives

Emerging technologies are revolutionizing the study of environmental-genetic interactions in aging by providing unprecedented resolution and integration of data. Multiomics approaches, particularly at the single-cell and spatial levels, are transforming aging research, enabling scientists to decode complex molecular networks that change with age and in response to environmental exposures [73]. Advances in epigenomics not only identify biomarkers of aging but also uncover reversible pathological epigenetic events (PEERs), opening avenues for targeted therapeutic interventions [74]. The integration of AI and machine learning with biosensors and bioengineering creates intelligent systems capable of real-time monitoring and modulation of environmental and biological signals influencing aging. Microfluidic organ-on-chip technologies also allow modeling of organ-specific aging and the effects of environmental stressors in controlled settings [75]. Collectively, these technologies enable more precise, personalized understanding and management of aging in the context of genetics and environment.

Potential interventions targeting environmental factors focus on modifiable lifestyle components such as diet, physical activity, and stress management, which epigenomic data suggest can decelerate biological aging. Engineered living therapeutics, including modified microbiota or cells producing beneficial compounds, offer sustainable, targeted interventions inside the body [76]. Regulatory peptides like GLP-1 analogs, initially developed for metabolic diseases, show promise as neuroprotective agents combating age-related cognitive decline linked to environmental stressors [77]. Green technologies and sustainable practices to reduce environmental pollutants also have downstream impacts on aging biology by minimizing oxidative and inflammatory burdens [14]. Nanotechnologies like nanozymes may serve as antioxidant or enzymatic therapies to counteract environmental insults driving aging processes.

The importance of multidisciplinary approaches integrating genetics, environmental science, biochemistry, computational

biology, and clinical research cannot be overstated. Aging is a complex, multifactorial process where genetic predispositions and cumulative environmental exposures converge to shape healthspan and longevity [78]. Efforts combining molecular biology, systems-level omics, environmental monitoring, epidemiology, and AI-driven data analytics are essential to unravel this complexity and translate findings into effective interventions [79, 80]. Such integrative frameworks facilitate personalized aging medicine and public health strategies to mitigate the impact of adverse environments while leveraging genetic resilience.

8. Conclusion

Environmental factors have profound impacts on genetic aging, shaping aging trajectories and the risk of age-related diseases. Comprehensive studies reveal that many age-related diseases and premature mortality are more strongly influenced by the exposome the cumulative measure of environmental exposures than by polygenic genetic risks alone. Key environmental exposures including smoking, socioeconomic status, physical activity, sleep quality, and early-life conditions collectively drive biological aging and morbidity through complex molecular pathways involving epigenetic modifications, inflammation, oxidative stress, and cellular senescence. These findings highlight that aging is a modifiable process shaped by the interaction of genetics and a wide range of environmental determinants, requiring integrative approaches to fully understand and intervene effectively.

The implications for aging research emphasize the need to integrate environmental and genetic data using multi-omics and advanced modeling techniques to dissect the mechanisms underlying aging and age-associated diseases. This integration facilitates identification of robust biomarkers predictive of biological age and exposome influences, guiding targeted interventions. Therapeutic strategies now focus on modifiable lifestyle factors, epigenetic reprogramming, and environmental risk reduction to promote healthy aging and mitigate disease burden. Model system studies remain indispensable, allowing controlled experiments that unravel molecular details of gene-environment interplay and validate potential therapies before translation to humans. Despite inherent limitations, these models provide essential tools to explore biological complexity and test interventions at cellular and organismal levels.

In conclusion, understanding the intricate relationships between environmental exposures and genetic factors in aging is crucial for developing personalized and population-level strategies to extend health span. Continued advancement in multi-disciplinary research, combining environmental science, genetics, molecular biology, and computational approaches, will drive innovative therapies and public health policies for aging populations worldwide.

Abbreviations

AMPK	AMP-Activated Protein Kinase
CRISPR	Clustered Regularly Interspaced Short Palindromic Repeats
INK	Inhibitor of Cyclin-Dependent Kinase
PEERs	Pathological Epigenetic Events
RNAi	RNA Interference
ROS	Reactive Oxygen Species
TOR	Target of Rapamycin

Author Contributions

Alebachew Molla is the sole author. The author read and approved the final manuscript.

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No new data were created or analyzed in this review.

Conflicts of Interest

The author declares no conflicts of interest.

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