The Epigenetics of Aging: Can We Reverse the Biological Clock?

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1 | INTRODUCTION

Aging can be defined as the continuous functional decline of a biological organism; however, there is an important distinction between chronological and biological age. Generally, we refer to a person's chronological age, and the distinction does not matter as biological age typically mirrors chronological age. However, in some cases, one's biological age can be accelerated or slowed in relation to their chronological age. There is currently no widely accepted, concrete method of measuring biological age, but it is often assessed using molecular factors like telomere length, cell senescence features, and epigenetic patterns (Field et al., 2018). Biological age is the best predictor of the consequences of aging, including disease susceptibility, and cognitive or physical deterioration. This is why understanding the molecular mechanisms behind the discrepancies between biological and chronological age is crucial (Musci et al., 2023).

Epigenetic factors in an organism are secondary to the DNA genome and often function to regulate gene expression. While our genomes are stable over time and see little modification, our epigenomes store information reversibly, and are constantly changing. In fact, significant gene expression changes can be detected within time periods as short as 12 hours, due to epigenetic variance (Oh et al. 2018). While chemical modifications of histone proteins are key epigenetic mechanisms, DNA methylation, particularly the conversion of cytosine to 5-methylcytosine (5mC), is the most prevalent (Soto-Palma et al., 2022; Field et al., 2018). Nearly all 5mC targets are found at CpG dinucleotides, which enable the preservation of methylation patterns through Dnmt1-mediated maintenance methylation during DNA replication and cell division (Breiling and Lyko, 2015). Cellular machinery can interact with methylated DNA using 'read, write and erase' mechanisms. This includes DNA methyltransferases (Dnmts), which establish methylation patterns; ten-eleven translocation (TET) enzymes, which remove methylation marks; and methyl-CpG-binding domain proteins, which recognize and interpret methylated nucleotides (Soto-Palma et al., 2022). CpG methylation patterns undergo significant changes during cell differentiation, as these patterns play a key role in determining a cell's

lineage commitment. CpG sites are unevenly distributed across the genome, with CpG-rich regions, known as CpG islands, commonly found in promoter regions. (Field et al., 2018; Soto-Palma et al., 2022). These islands are preserved because meCpG sites are prone to deamination, producing TG dinucleotides. Since promoter regions are typically unmethylated, their CpG dinucleotides can remain intact, whereas methylation in other genomic regions increases the likelihood of meCpG deamination and an overall loss of CpG dinucleotides. (Soto-Palma et al., 2022).

Epigenetic changes, specifically in DNA methylation, regulatory RNA activity, histone modification, and chromatin remodeling, are established hallmarks of aging (Wang et al. 2022). Models based on single biomarkers, blood pressure for example, have been attempted as predictors of biological age, but were not shown to be robust (Field et al., 2018; Musci et al., 2023). The most common and accurate predictors have now been identified as epigenetic models, which look primarily at the unique methylation patterns of DNA. These 'epigenetic clocks' are developed by identifying the methylation patterns of certain CpG sites whose methylation shows the greatest correlation to chronological age (Field et al., 2018; Horvath, 2013). The most widely cited epigenetic clock was published in 2013 by Horvath and reports a high correlation coefficient of 0.97 between DNA methylation and chronological age. Significant deviations between chronological and biological age are uncommon and often signal underlying disease, suggesting epigenetic clocks are essential for detecting such discrepancies and predicting age-related disease.

DNA damage is also highly correlated to the effects of aging, and Soto-Palma et al. (2022) suggest there are important interactions between epigenetic markers and DNA damage. DNA damage is a major risk factor for a variety of prevalent age-associated diseases such as cancer, cardiovascular disease, neurodegeneration, and diabetes (Plesa et al., 2023). These diseases can lead to a decline in the quality of life of the elderly population by reducing personal autonomy and independence (Plesa et al., 2023). Present social and economic challenges associated with aging are becoming a rapidly increasing problem (Figure 1). Moreover, the elderly population is expected to double by the end of the century, further exacerbating the issue (Plesa et al., 2023). Therefore, it is important to understand the processes behind aging and to study potential therapies to reverse age-related decline. Analysis of epigenetic changes and

epigenetic clocks are likely the best predictors of biological age and given the amount of interaction between aging and the epigenetic landscape, epigenetic targets are the most promising for the development of anti-aging therapies.

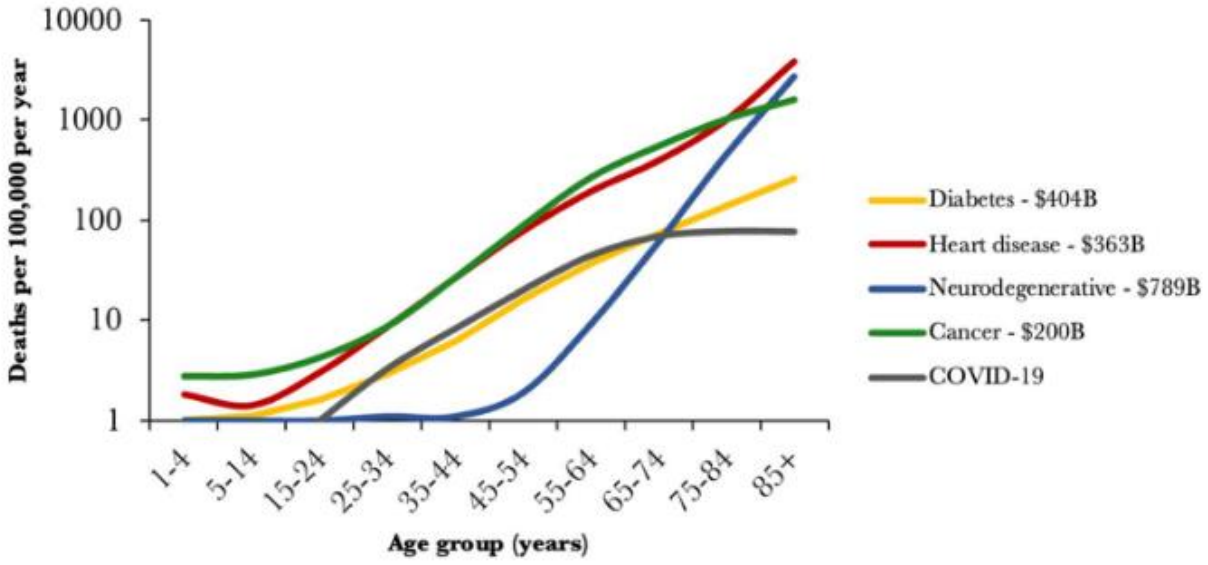

Figure 1. U.S. Death rate per 100,000 people per year for leading causes of death across multiple age groups. The data for diabetes, heart disease, neurodegenerative, and cancer was compiled as of 2019, while the COVID-19 deaths are for 2020-2021. The estimated associated healthcare costs for diabetes, heart disease, and neurodegenerative diseases (2017), and cancer (2020) are also reported (Plesa et al., 2023).

1.1 | Epigenetic Mechanisms Driving Aging

Aging is strongly influenced by changes in epigenetic regulation, including alterations in chromatin structure, histone modifications, and DNA methylation. An increase in chromatin accessibility, caused by histone loss and the incorporation of unstable histone variants, leads to abnormal upregulation of specific genes (Saul & Kosinsky, 2021). This open-chromatin state increases the likelihood of aberrant gene activation, which has been closely linked to age-associated diseases such as cancer and neurodegenerative disorders. Conversely, site specific hypermethylation is also observed, especially on promoter CpG islands, leading to a more closed chromatin structure and transcriptional silencing of certain genes, as illustrated in Figure 2 (Wang et al., 2022). In contrast, demethylation of CpG dinucleotides is linked to transcriptional

activation (Demidenko et al., 2021). Field et al. (2018) describes the overall methylation landscape as “smoothening” with age, where high and low level meCpGs progress to an intermediate methylation pattern closer to 50%. This is the opposite observation as that of early development, where entropy in the epigenome is high.

Aging is associated with a variety of epigenetic changes that contribute to its detrimental effects. Among these changes, DNA methylation is the most extensively studied epigenetic marker of aging. It typically involves the DNA methyltransferase (Dnmt) catalyzed conversion of cytosine residues to 5-methylcytosine (5mC). As described by Wang et al. (2022), age-related changes in Dnmt expression, particularly decreased activity of Dnmt1, which maintains existing methylation patterns, lead to global genomic hypomethylation over time. These molecular alterations contribute to reduced variation in the epigenome and more open chromatin structure in aged cells compared to early development stages.

In addition to methylation changes, DNA damage also plays a causal role in aging, and age-related diseases, particularly cancer (Soto-Palma et al., 2022). DNA damage and epigenetic regulation are largely intertwined. Spontaneous DNA damage caused by oxidative stress, chemical stress, or other factors form DNA lesions, which can halt replicative and transcriptional polymerases and activate the DNA damage response (DDR). This pathway halts the cell cycle and attempts to repair the lesion. The DDR is an opportunity for cell fate determination, where induction of apoptosis or senescence may occur. This response could also signal for epigenetic alteration at the damaged site. Interestingly, DNA methylation itself can also promote DNA damage, since oxidation of 5mC by TET enzymes can produce 5-hydroxymethylcytosine (5hmC). 5hmC may play a role in identifying DNA sites as damaged and is a target for base excision repair. Over a lifetime, the accumulation of millions of DDR events per cell contributes to aging effects by increasing the proportion of unviable or senescent cells and promoting transcriptional heterogeneity of the epigenome as described above (Soto-Palma et al., 2022).

Experimental evidence further supports the link between DNA damage and epigenome heterogeneity. In a mouse model, Russo et al. (2016) induced double-stranded breaks at a common genomic locus and observed, following homologous recombination repair, different cells exhibited distinct methylation and histone modification patterns. These differences led to variable transcriptional outcomes, demonstrating that DNA repair processes can directly reshape

the epigenetic landscape. However, when analyzed through epigenetic clock models, results remain mixed regarding whether DNA damage accelerates biological aging (Soto-Palma et al., 2022).

Together, these findings highlight that while epigenetic drift is an inevitable consequence of aging, its underlying mechanisms are dynamic and reversible. Understanding how DNA methylation, chromatin remodeling, and damage-repair pathways interact offers a promising approach for developing targeted epigenetic interventions to restore youthful gene regulation and mitigate age-related cellular decline.

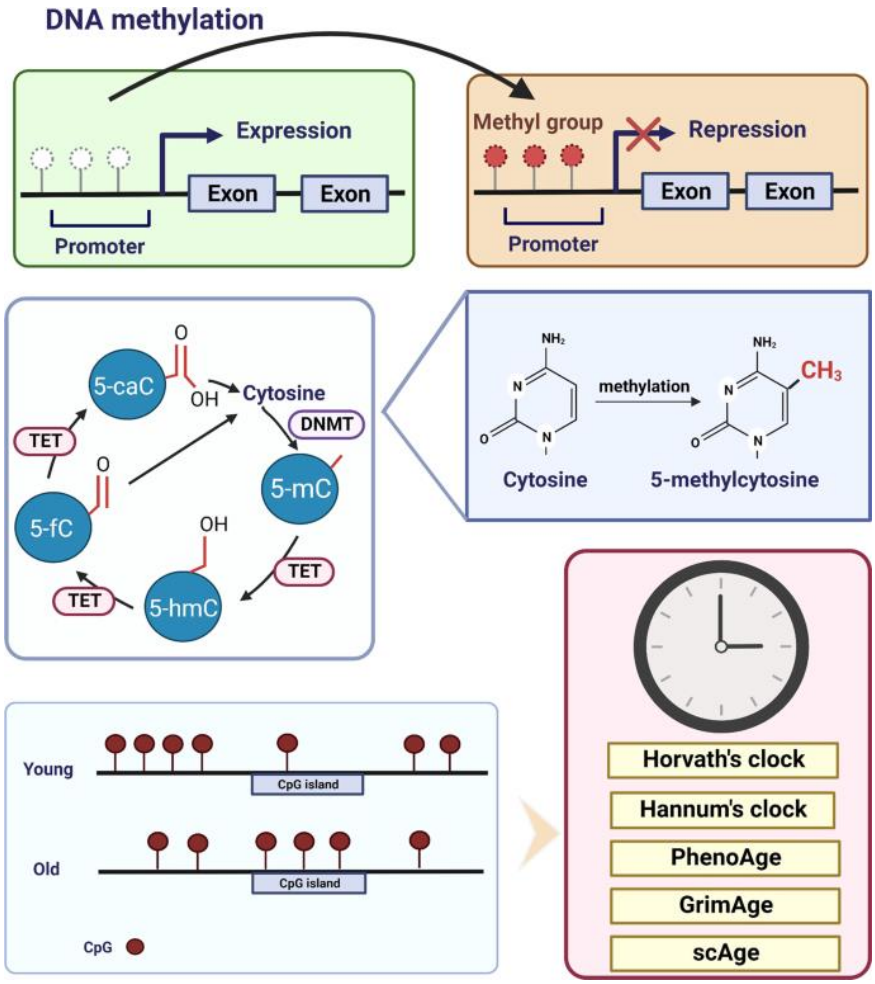

Figure 2. The mechanism of DNA methylation and the epigenetic clock theory of aging (Wang et al., 2022).

1.2 | Age Associated Diseases and Diagnostic Potentials

Beyond general aging, epigenetic alterations serve as early biomarkers for many age-related diseases, including Alzheimer's disease, diabetes, and cardiovascular disorders. According to Galow and Peleg (2022), specific DNA methylation patterns, particularly in genes such as ANK1, are consistently altered in Alzheimer's patients. Notably, these changes arise before the appearance of clinical symptoms, highlighting the value of epigenetic tracing as a diagnostic tool for early disease detection.

Epigenetic mechanisms can also influence the expression of circadian clock genes, which regulate metabolic and neuronal homeostasis. Methylation changes affecting transcription factors such as Brain and Muscle Arnt Like 1 (BMAL1) and Circadian Locomotor Output Cycles Kaput (CLOCK) have been associated with the onset of neurodegenerative diseases (Latha Laxmi & Tamizhselvi, 2024). In mice models of Alzheimer's and Parkinson's disease, both DNA methylation of circadian genes and altered expression of BMAL1 and CLOCK were observed, further linking circadian dysregulation to epigenetic aging (Latha Laxmi & Tamizhselvi, 2024).

Building upon these observations, Izquierdo et al. (2025) investigated the relationship between epigenetic acceleration of biological age and obesity. Obesity shares many molecular hallmarks with biological aging, including chronic inflammation, oxidative stress, and mitochondrial dysfunction. Using three different epigenetic clocks, the researchers demonstrated that individuals with obesity exhibited a significantly higher biological age compared to healthy individuals. In fact, obesity was found to exacerbate epigenetic changes typically associated with aging. This resulted in an observed 2.7-year acceleration in biological aging for every 10-point increase in body mass index (Izquierdo et al., 2025). These findings emphasize that obesity not only mimics but also amplifies age-related epigenetic changes, supporting the value of epigenetic clocks for early prognosis.

The development of an epigenetic clock was one of the first steps in determining biological age, and there are now many models which show high correlation to chronological and biological age. Horvath's "epigenetic clock" was developed using DNA methylation data from over 7,000 samples representing 51 different human tissues and cell types. Using an elastic net regression model, Horvath (2013) identified 353 CpG sites whose methylation levels change predictably with chronological age. Each CpG site was assigned a weight, and the weighted

average of these methylation values produces a DNA methylation age (DNAm age). To account for the faster rate of epigenetic changes early in life, the model applies a transformation that is logarithmic during development and linear in adulthood.

The resulting DNAm age correlates strongly with chronological age across tissues. Methylation values at the 353 CpG sites can be extracted from patient samples, multiplied by their corresponding weights, and summed to yield a predicted biological age. The difference between DNAm and chronological age, known as age acceleration, serves a quantitative measure of biological aging. Horvath's analyses revealed that epigenetic aging occurs rapidly during early development and slows in adulthood. Furthermore, stem cells display near-zero DNAm age, while many cancer tissues exhibit substantial age acceleration, suggesting a disruption in normal epigenetic maintenance. Collectively, the epigenetic clock supports the concept that DNA methylation patterns reflect fundamental biological processes of aging, making it a valuable biomarker of biological age (Horvath, 2013).

Overall, advances in the analysis of epigenetic clocks and related biomarkers hold great promise for the future of personalized anti-aging and preventative medicine. As the precision of methylation-based diagnostics improves, these tools may allow clinicians to not only detect but also quantitatively track biological aging, offering new strategies to delay or reverse age-associated disease progress.

1.3 | Experimental Evidence and Methodologies of Potential Anti-Aging Therapies

To determine whether the epigenetic trends responsible for aging are reversible, researchers have turned to cellular reprogramming experiments. Takahashi and Yamanaka (2006) demonstrated that differentiated adult cells could be reprogrammed back into induced pluripotent stem cells (iPSCs) using four transcription factors, Oct4, Sox2, Klf4, and c-Myc (OSKM), now collectively known as the Yamanaka factors. This full cellular reprogramming essentially resets the epigenetic clock, erasing all markers of cellular aging. Methodologically, the researchers used gene transfection to overexpress OSKM factors in fibroblasts and monitored epigenetic age reversal through methylation clocks and chromatin accessibility assays. However, one limitation of this strategy was that some cells may be fully reversed to iPSCs, making it improbable to delay aging in vivo due to the teratoma-forming ability of these stem cells. Although this method

offers a potential route to reverse cellular aging, it must be further studied to ensure that cells can be safely reprogrammed without the potential of full dedifferentiation. As a result, partial reprogramming has emerged as a safer approach, allowing for rejuvenation without full dedifferentiation. This technique demonstrates that epigenetic age is not fixed, providing an approach to regenerative medicine and anti-aging therapies.

An example of this approach comes from Lu et al. (2020), where eyesight was restored in a mouse model of glaucoma through partial reprogramming. As shown in Figure 3, by ectopically expressing Oct4, Sox2, and Klf4 (OSK), excluding c-Myc, the researchers reinstated youthful DNA methylation and transcriptomic patterns in retinal ganglion cells, reversing vision loss. While long-term reprogramming can rejuvenate aged cells, it also risks generating iPSCs capable of forming teratomas. To address this, transient reprogramming, in which reprogramming factors are expressed for limited time periods, has shown promise. Transfection of aged human fibroblasts, chondrocytes, and endothelial cells with mRNAs encoding OSKM, LIN28, and NANOG (OSKMLN) rejuvenated host cells and significantly reversed their epigenetic age. Both long-term and transient cellular reprogramming can achieve rejuvenation, but the transient method offers a safer, controlled strategy for in vivo application.

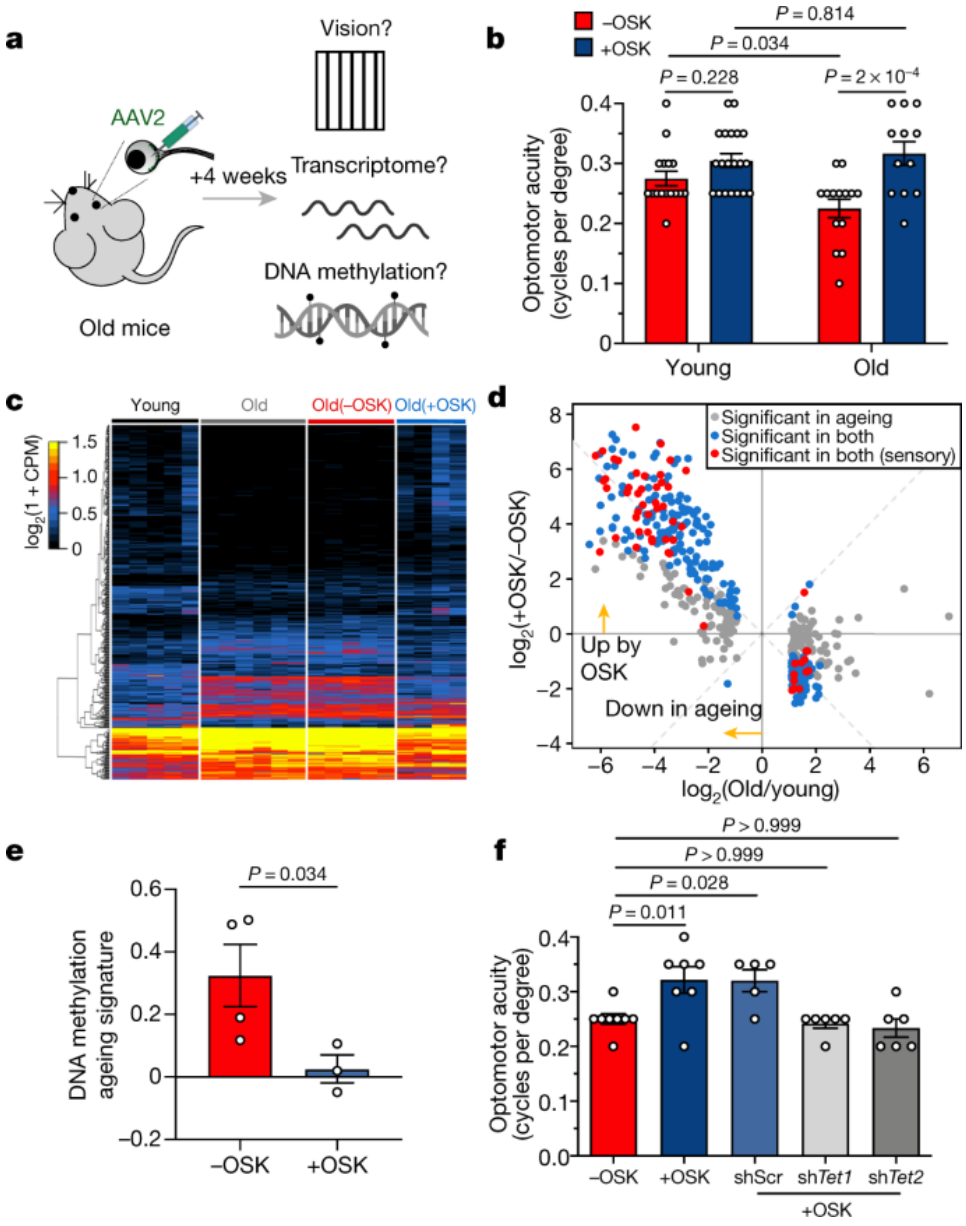

Figure 3. **a**, Experimental outline for testing the effect of reprogramming in old mice. **b**, Visual acuity in young (4-month-old) and old (12-month-old) mice after 4 weeks of −OSK or +OSK. **c**, **d**, Hierarchical clustered heat map (**c**) and scatter plot (**d**) showing mRNA levels of 464 genes that were differentially expressed between young and old RGCs and the effect of OSK. **e**, DNA methylation ageing signatures of RGCs from 12-month-old mice infected for 4 weeks with −OSK or +OSK. **f**, Visual acuity in old (12-month-old) mice treated for 4 weeks with −OSK, +OSK, or +OSK together with short hairpin scramble RNA (shScr), shTet1 or shTet2 (n = 8, 7, 5, 6 and 6 eyes, respectively (Lu et al., 2020).

Expanding on these findings, Plesa et al. (2023) introduced the concept of transcriptomic reprogramming, defined as the transition between two defined transcriptomic states using specific genetic mutations. Their work proposed a novel method for identifying potential age-reversal genetic targets through mutation-based transcriptomic reprogramming screens. The approach begins with transcriptomic profiling of primary cells from donors of varying ages to identify age-associated expression patterns. Candidate genes are mutated, and the resulting changes in the aging phenotype are evaluated through transcriptomic analyses. The most promising targets are subsequently validated in cell type specific functional assays (Plesa et al., 2023).

Neurons represent a particularly promising cell type for such research. Not only is age-reversal in neurons a potential treatment for delaying cognitive decline and neurological movement disorders, but neurons are also particularly relevant to study as these non-dividing cells face the unique challenge of maintaining genome and epigenome stability over their long cellular life (Plesa et al., 2023). However, studying primary neurons is complex due to difficulty maintaining them in culture. Methods using induced pluripotent stem cells and subsequent differentiation into neurons is promising, but as mentioned previously, the dedifferentiation process erases all markers of cellular aging. Therefore, while these methods are promising for modelling the aging phenotypes in neurons they are not fully able to capture true aging in vivo (Plesa et al., 2023).

A different method for modelling aging neurons for study is the transdifferentiation model, in which specific somatic cell types are directly converted into neurons without passing through a pluripotent intermediate state. This preserves both transcriptomic and DNA methylation signatures of aging, enabling the study of true aging phenotypes in vitro (Plesa et al., 2023). The transdifferentiation model has proved successful in converting human fibroblasts directly into various neuronal and glial cell types, providing a valuable tool for studying neuronal aging and testing rejuvenation strategies. Additionally, transcriptomic reprogramming of neurons to restore youthful activity patterns shows promise for reversing cognitive decline as a consequence of natural aging (Plesa et al., 2023).

1.4 | Pharmacological and Lifestyle Interventions can Slow Biological Aging

Emerging therapies aim to manipulate epigenetic pathways to slow or even reverse aging. Several promising interventions are outlined by Saul & Kosinky (2021) and by Wang et al. (2022) and shown in Figure 4. These include the use of histone deacetylase (HDAC) inhibitors to promote chromatin relaxation, Dnmt inhibitors to prevent hypermethylation of specific promoter regions, and drugs targeting ATP-dependent chromatin remodelers such as the SWI/SNF complex to correct nucleosome positioning. Other approaches involve senolytic drugs that selectively eliminate senescent cells, thereby reducing inflammation and pro-aging signals.

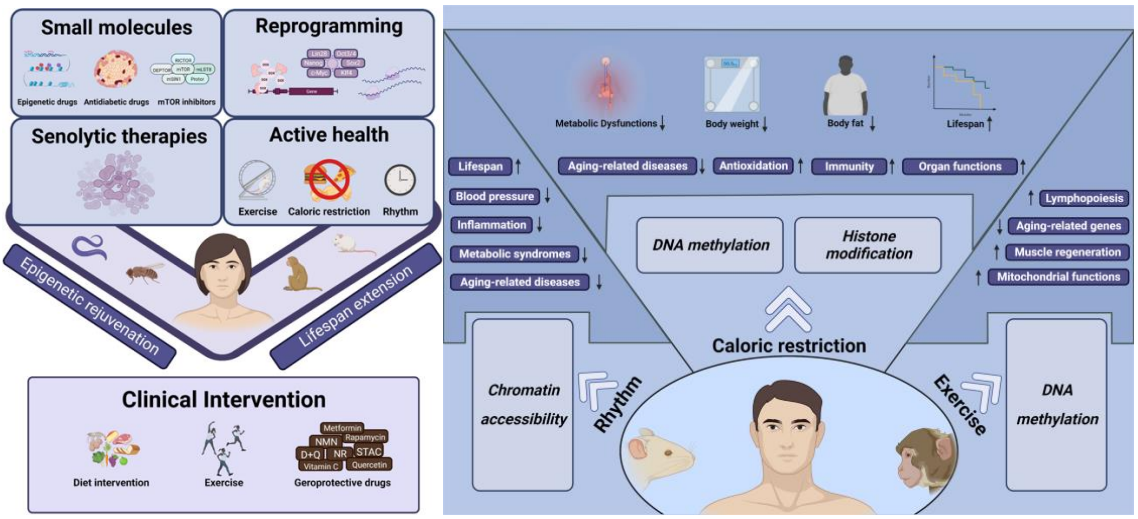

Figure 4. Intervention strategies that alleviate cellular aging (Wang et al., 2022).

Among the anti-aging compounds discovered to date, alpha-ketoglutarate (AKG) is one of the most promising. AKG, an intermediate metabolite naturally found as part of the Krebs cycle, participates in multiple metabolic pathways and cellular processes, serving as a signalling molecule, precursor for amino acid synthesis, and epigenetic regulator. However, during aging, the endogenous levels of AKG naturally decline, a trend exacerbated by impaired mitochondrial function. In a study by Demidenko et al. (2021), the link between the epigenetic clock, physical fitness, and the effects of taking Rejuvant, a calcium AKG-containing drug, was investigated. In the study 42 participants without any chronic medical conditions elected to take Rejuvant for 7 months. The participants biological age was measured using the TruAge methylation test, which

examined a small number of methylation sites in CpG islands. Although this test examines a smaller portion of the genome than other epigenetic clocks, it provides a more affordable approach. The results of the study, as shown in Table 1, revealed an average decrease of approximately eight years in biological age after treatment ($p = 6.538 \times 10^{-12}$). While these findings are promising and suggest Rejuvant or other drugs containing calcium AKG may have significant positive effects on biological age, the absence of a placebo control group, small sample size, and reliance on saliva methylation data for determining biological age highlight the need for further large-scale validation studies (Demidenko et al., 2021).

Table 1. Descriptive characteristics of participants before and after treatment in a study conducted by Demidenko et al.

Total Participants	42
Gender (Female/ Male)	14/ 28
Female:	
Chronological Age (median; range)	64.09; 43.49 to 72.46
Biological Age at Baseline (median; range)	62.15; 46.4 to 73
Biological Age at T7* (median; range)	55.55; 33.4 to 63.7
Male:	
Chronological Age (median; range)	62.78; 41.31 to 79.57
Biological Age at Baseline (median; range)	61.85; 41.9 to 79.7
Biological Age at T7* (median; range)	53.3; 33 to 74.9

*Indicates biological age as measured by TruMe test after an average of seven months of treatment.

Lifestyle interventions, such as calorie restriction, exercise, and circadian rhythm regulation also beneficially regulate epigenetic markers. Variation in the expression of circadian clock genes can be impacted by substance use, including alcohol, cocaine, drugs, and smoking, as well as food habits and sleep patterns (Latha Laxmi & Tamizhselvi, 2024). For instance, six hours of sleep deprivation alters chromatin accessibility in the cerebral cortex of mice, contributing to long-term effects on gene expression (Hor et al., 2019). Similarly, calorie and methionine restriction in animal models have been shown to reduce biological age (Johnson et al., 2022).

In individuals with clinical obesity, Izquierdo et al. (2025) observed that introducing a very low-calorie ketogenic diet (VLCKD) produced a partial reversal of the accelerated biological aging typically seen in patients with the disease, as shown in Figure 5. After only 30 days following VLCKD intervention, participants exhibited an average 6.1-year decrease in DNA methylation-based biological age. This reduction correlated with increased levels of ketone bodies and altered methylation of genes regulating adipose tissue, neurological functioning, and muscle development. Overall, their findings supported VLCKD as a treatment for obesity due to its capacity to modulate biological aging through epigenetic mechanisms highlighted in Figure 6. However, it is important to note that this study had several limitations, including a small sample size of only 10 participants. They also followed the nutritional intervention for a short time span of 6 months. Additionally, all participants were European Caucasians. Further studies investigating the effects of the VLCKD diet on biological aging over long periods of time with a larger, more diverse sample size are necessary (Izquierdo et al., 2025).

Environmental factors have also been found to play a significant role in accelerating biological aging. Schmidt (2024) reported that higher pollutant exposure was associated with an increase of 2.2 years in biological age. Furthermore, disruption of circadian rhythms through shift work elevates the risk of age-associated diseases (Latha Laxmi & Tamizhselvi, 2024). These findings, along with many other studies listed in Table 2, emphasize the various factors playing a role in biological aging and the potential of targeted pharmacological and lifestyle interventions to decelerate or even reverse its molecular hallmarks.

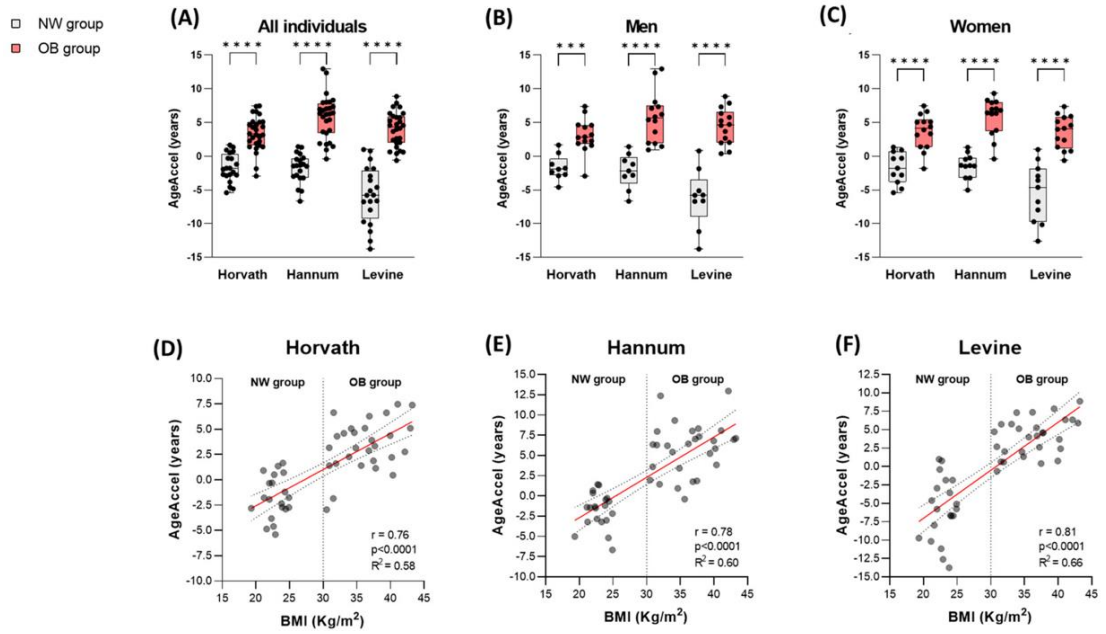

Figure 5. Differences in chronological and biological age of patients with normal weight (NW) and obesity (OB) determined by three different epigenetic clocks (Izquierdo et al., 2025).

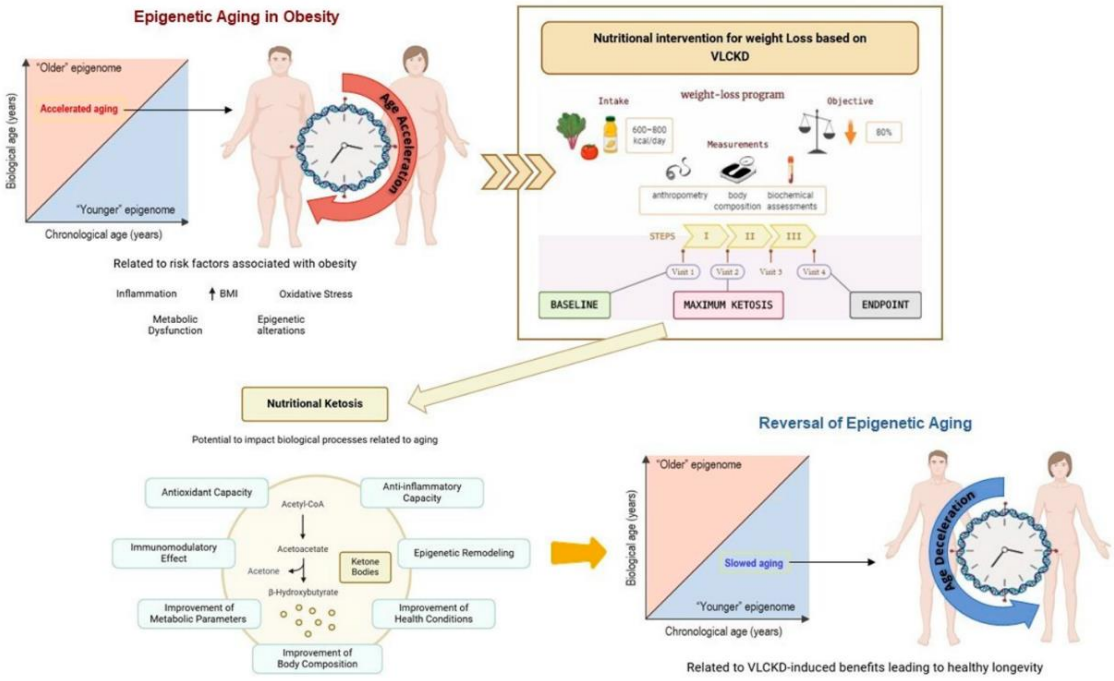

Figure 6. Schematic representation illustrating the possible mechanistic link between metabolic improvements derived from nutritional ketosis induced by VLCKD and the slowing of obesity-related epigenetic aging (Izquierdo et al., 2025)

Table 2. Studies ranging from 2017 to 2021 that focused on dietary, lifestyle, and pharmacological interventions reported to slow or reverse an aging clock in humans (Johnson et al., 2022).

Intervention	Result	Aging clock used	Subject #	Health status	Age information (years)	Study reference
25% caloric restriction	Compared to the ad-libitum group, the caloric restriction group was **0.6** years younger after **24 months**	Klemera-Doubal Method (Klemera & Doubal, 2006)	220	Non-obese	21–50	Belsky et al. (2017)
Metformin, growth hormone, and dehydroepiandrosterone	Compared to baseline, epigenetic age was decreased by **2.16** years after **12 months**	GrimAge (A. T. Lu, Quach, et al., 2019)	10	Healthy	51–65	Fahy et al. (2019)
Vitamin D3	2000 IU/day of vitamin D3 for **16 weeks** decreased epigenetic age by **1.9** years compared to placebo	Hannum (Hannum et al., 2013)	51	Overweight or obese with low vitamin D status	26.1 ± 9.3	L. Chen et al. (2019)
Bariatric surgery	**12 months** post-surgery, Δage decreased by **0.92** years	Horvath (Horvath, 2013)	40	Severe obesity	45.1 ± 8.06	Fraszczyk et al. (2020)
Mediterranean-like diet	In Polish subjects, Δage was **0.84** years less than it was pre-intervention **12 months** prior	Horvath (Horvath, 2013)	120	Healthy	65–79	Gensous et al. (2020)
Antiretroviral therapy	Drug treatment for **96 weeks** decreased Δage by **3.6** years	PhenoAge (M. E. Levine et al., 2018)	168	HIV	30–46	Esteban-Cantos et al. (2021)
Plant-based diet	Relative to controls, Δage was reduced by **0.66** years after **24 months**	GrimAge (A. T. Lu, Quach, et al., 2019)	219	Healthy	50–69	Fiorito et al. (2021)
Plant-centered diet, supplements, exercise, sleep, and stress management	Compared to controls, an **8-week** intervention decreased epigenetic age by **3.23** years	Horvath (2013)	43	Healthy	50–72	Fitzgerald et al. (2021)
Diet (low-fat or Mediterranean/ low-carbohydrate) and physical activity	Compared to individuals that failed to lose weight, subjects that successfully lost weight were **0.5** years younger after **18 months**	J. Li et al. (2018)	120	Obesity or dyslipidemia	48.6 ± 9.3	Yaskolka Meir et al. (2021)

2 | CONCLUSION

The study of aging through epigenetics has transformed our understanding of biological age. While chronological age offers only a superficial measure of time, biological age, reflected in epigenetic patterns, serves as a far more accurate predictor of health status and disease susceptibility. The development of epigenetic clocks, particularly Horvath's model, has enabled researchers to quantify biological age with high precision, revealing that deviations between biological and chronological age often indicate underlying disease or accelerated aging.

Epigenetic biomarkers are now being used to detect preclinical stages of diseases such as Alzheimer's, diabetes, and obesity, signifying their diagnostic and prognostic potential. Epigenetic changes such as global DNA hypomethylation, histone loss, and chromatin remodeling drive much of the cellular dysfunction associated with aging. Importantly, these changes are reversible. Experimental breakthroughs in cellular and transcriptomic reprogramming, from Yamanaka factor-induced rejuvenation to transient reprogramming and direct transdifferentiation, demonstrate that cellular aging can be reset and modelled, offering therapeutic potential for regenerative medicine.

Emerging interventions, including pharmacological agents like HDAC and Dnmt inhibitors, AKG drugs, and dietary restrictions, further highlight the ability to modulate biological aging through lifestyle-based and molecular strategies. Environmental and behavioural factors, including sleep quality, circadian rhythm stability, and pollution exposure, also exert measurable effects on the epigenome, emphasizing the intricate interaction between external conditions and molecular aging mechanisms.

Overall, the epigenetic regulation of aging represents one of the most promising ways of detecting, understanding, and reversing biological aging. By identifying and manipulating the molecular mechanisms that underlie age-associated decline, researchers are advancing the use of personalized anti-aging medicine aimed at not only extending the lifespan, but prolonging healthspan and reducing the socioeconomic burden of age-related diseases.

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