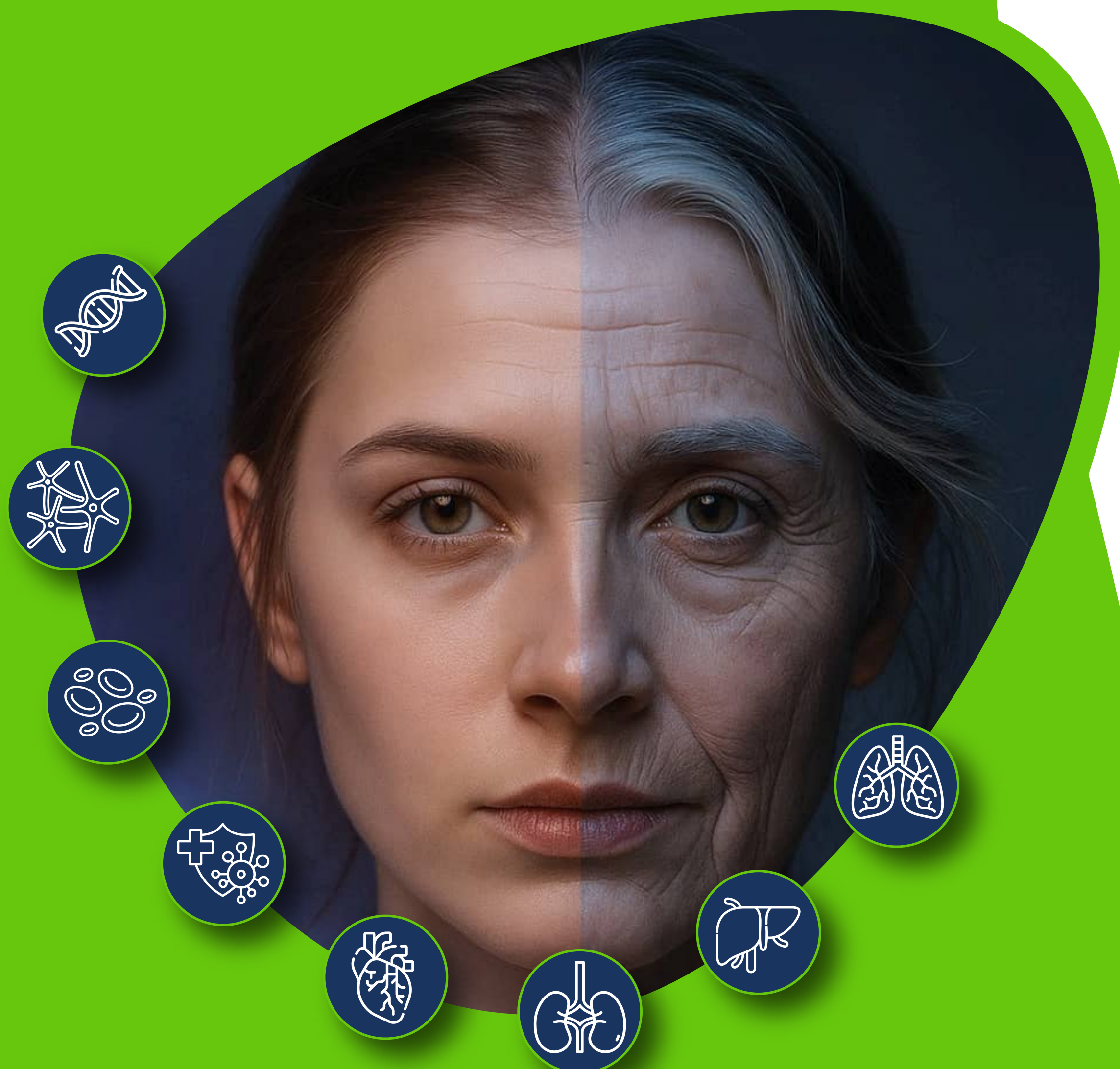

Epigenetics Biological Age Report

DISCOVER THE AGE YOUR BODY THINKS YOU ARE

Ordering Provider: **Doogie Howser**
Accession Number: **EM-DEMO**

Patient Name: **John Doe**
Patient Gender: **Male**
DOB: **03/03/1983**

Collected Date: **01/01/2025**
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Table of Content

Introduction

Biological age is a dynamic indicator of health that reflects how well your body is functioning relative to your chronological age. Through epigenetics, the science of how environmental and lifestyle factors influence gene activity, we gain a unique insight into aging processes. DNA methylation, the most widely studied epigenetic mechanism, affects gene expression and is used here to measure biological function in specific systems such as brain and cognitive, vision wellness, and immune function.

Visual function is a sensitive indicator of neurovascular and retinal aging; cognitive performance reflects neuronal integrity, synaptic plasticity, and resilience to neurodegeneration; and immune system aging (immunosenescence) is strongly linked to increased risk for chronic inflammation, infection, and age-associated diseases. Together, these domains offer clinicians a systems-level perspective to evaluate biological aging and guide targeted interventions to promote healthy longevity.

Understanding Epigenetics: A Scientific Overview

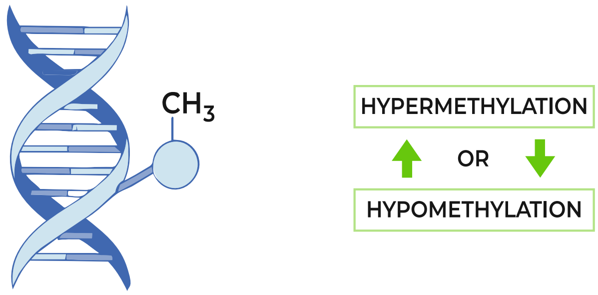
The field of genomics has advanced considerably beyond the completion of the Human Genome Project, ushering in the era of epigenetics, the study of heritable changes in gene function that do not involve alterations in the underlying DNA sequence. The term **epigenetics**, derived from the Greek prefix **"epi"** meaning upon or above, refers to mechanisms that regulate gene activity in response to environmental and lifestyle factors.

One of the most studied epigenetic mechanisms is **DNA methylation (DNAm)**. This process involves the addition of methyl groups to DNA, primarily at cytosine-phosphate-guanine (CpG) sites. These chemical modifications can either promote or suppress gene expression, depending on their location and context within the genome. As individuals age, methylation patterns shift, either becoming **hypermethylated** (increased methylation) or **hypomethylated** (decreased methylation), across various genomic regions. These alterations can impact biological functions such as memory, hearing, and vision.

While physical appearance or performance (e.g., muscle tone, speed, or dietary habits) may imply good health, such external markers are not always reliable indicators of internal physiological integrity. Likewise, possessing a favorable genetic profile does not guarantee health span or longevity. Instead, **epigenetic modifications** act as a critical interface between our genes and lifestyle, reflecting how factors like nutrition, physical activity, stress management, and sleep quality influence biological processes over time.

EPIGENETICS

BEYOND GENOMICS



DNA METHYLATION

Addition of methyl groups to DNA primarily at Cytosine-p-Guanine (CPG) sites as methylation patterns shift, resulting in hypermethylation or hypomethylation.

WELLNESS & AGING

Epigenetic modifications act as critical interface between our lifestyle factors such nutrition, physical activity, stress management, and sleep with biological processes.

Chronological vs. Biological Age

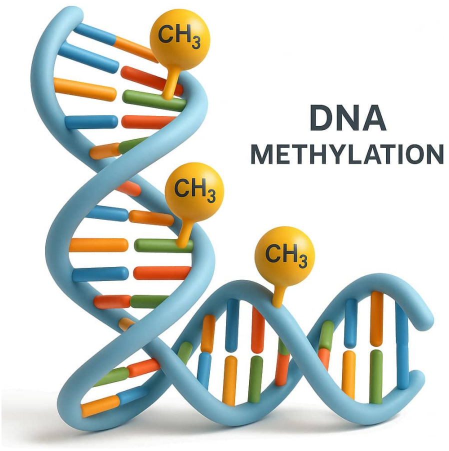
- **Chronological Age** refers to the number of years a person has lived since birth.
- **Biological Age** (e.g. vision wellness age, brain and cognitive age, and immune system integrity age) is determined using DNA methylation scores in genes associated with specific physiological domains. These biological age estimates may be younger or older than chronological age depending on gene expression and methylation patterns.

CHRONOLOGICAL AGE

BIOLOGICAL AGE

What is a Methylation Score?

A **methylation score** is a composite metric derived from the average methylation levels across a curated set of CpG sites related to specific biological functions. A methylation score distills complex epigenetic information into a single, interpretable value by combining methylation levels at a targeted collection of CpG sites linked to vital cellular processes. Through sophisticated weighting and normalization, it captures subtle shifts in gene-regulatory landscapes, offering a sensitive indicator of biological state. Elevated scores reflect coordinated methylation patterns that promote healthy gene activation and maintenance of genomic integrity. Conversely, lower scores can reveal early signs of epigenetic drift or disease-associated dysregulation. By compressing multidimensional methylation data into a standardized metric, this score facilitates cross-sample comparisons, longitudinal monitoring, and the identification of epigenetic biomarkers for research and clinical applications.

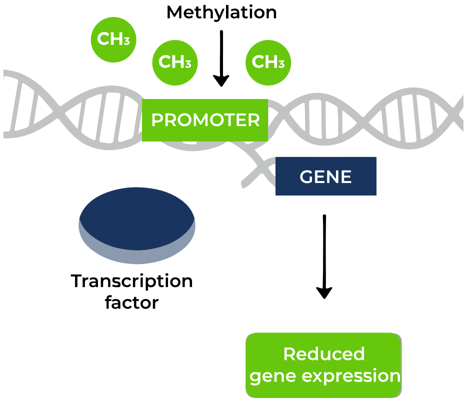


Each domain-specific algorithm categorizes results across **three expression bands**, ranging from poor to good, based on health data and gene expression patterns within population datasets.

If a date of birth is provided, an **epigenetic health age**, such as **vision wellness age, brain and cognitive age, and immune system integrity age** can be calculated. This value provides a comparative biological measure that indicates whether gene expression in that area is age-appropriate, accelerated, or delayed.

Impact of Methylation on Gene Expression

Methylation most frequently occurs in the promoter methylation regions, which regulate gene transcription. When these regions are methylated, transcription factors and other regulatory proteins are unable to bind efficiently, resulting in reduced or silenced gene expression — a phenomenon known as gene silencing. This process plays a crucial role in age-related decline and disease susceptibility.



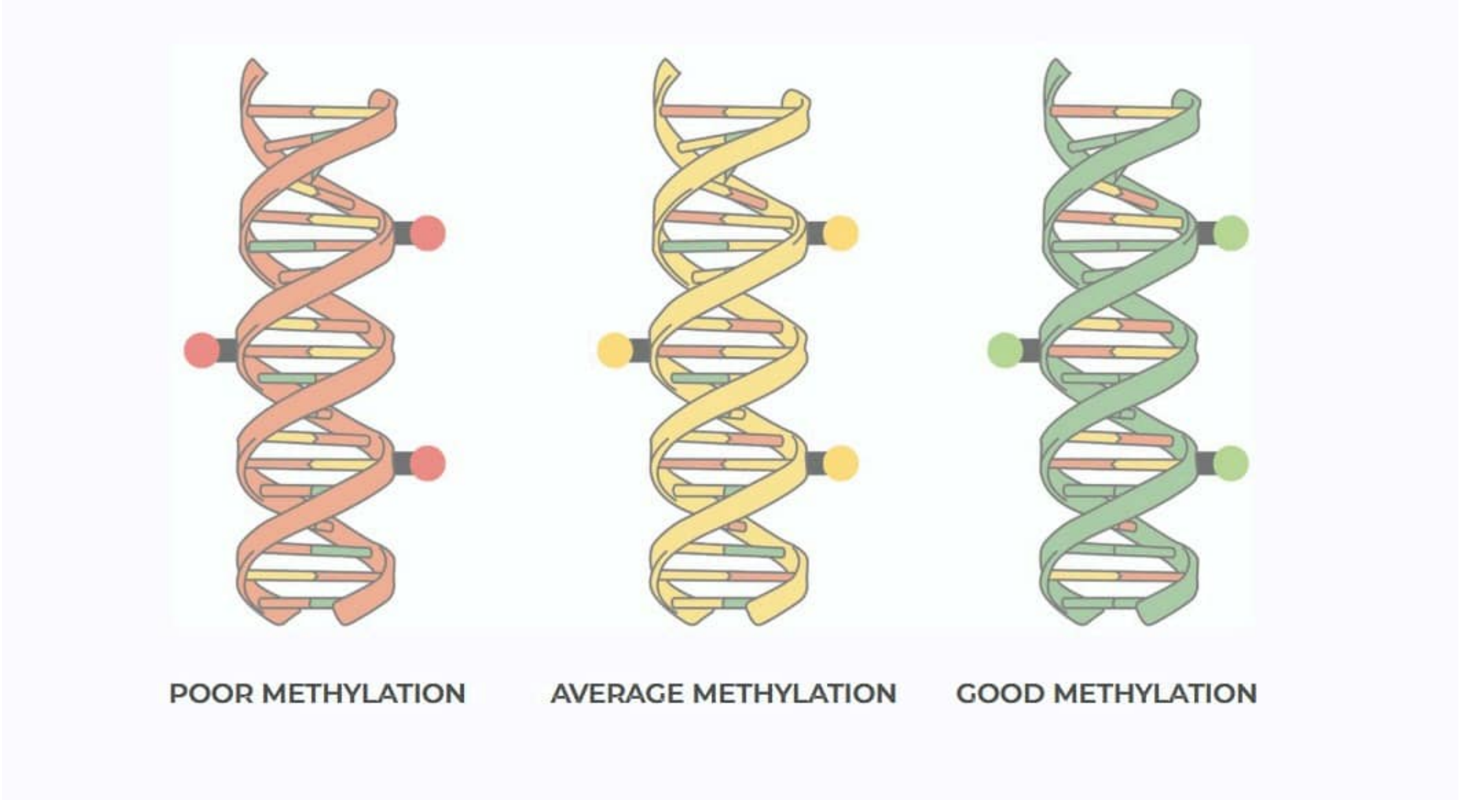
Epigenomic Status Snapshot

The **Epigenomic Status Snapshot** provides a functional snapshot of gene expression status across selected targets. Each gene is classified into one of three categories:

- **Good Methylation:** Indicative of favorable methylation and gene function.
- **Average Methylation:** Indicative of moderate methylation and gene function.
- **Poor Methylation:** Suggests potential dysregulation or suboptimal gene activity.

Classification Criteria-

- **Good (Methylated) : mean(beta) > 0.7 % Methylation > 70%**
- **Average (Partially Methylated) : mean(beta) 0.3-0.7 % Methylation 30–70%**
- **Poor (Unmethylated) : mean(beta) < 0.3 % Methylation < 30%**



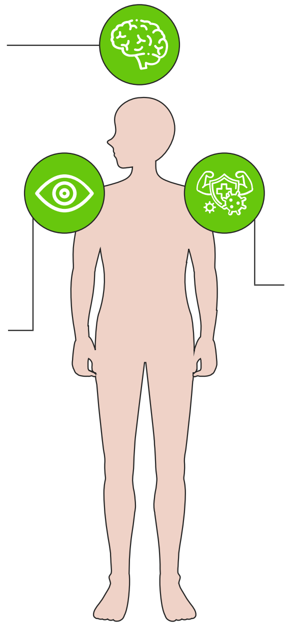
Epigenetic Biomarkers for Biological Age

Brain and Cognitive Age

Brain and cognitive age reflects how well memory, attention, learning, and executive functions are aging. Methylation patterns in genes tied to neurodegeneration, synaptic function, and plasticity help identify early cognitive decline — often before symptoms appear. This enables timely interventions to support long-term brain health and distinguish normal aging from early signs of conditions like Alzheimer's.

Vision Wellness Age

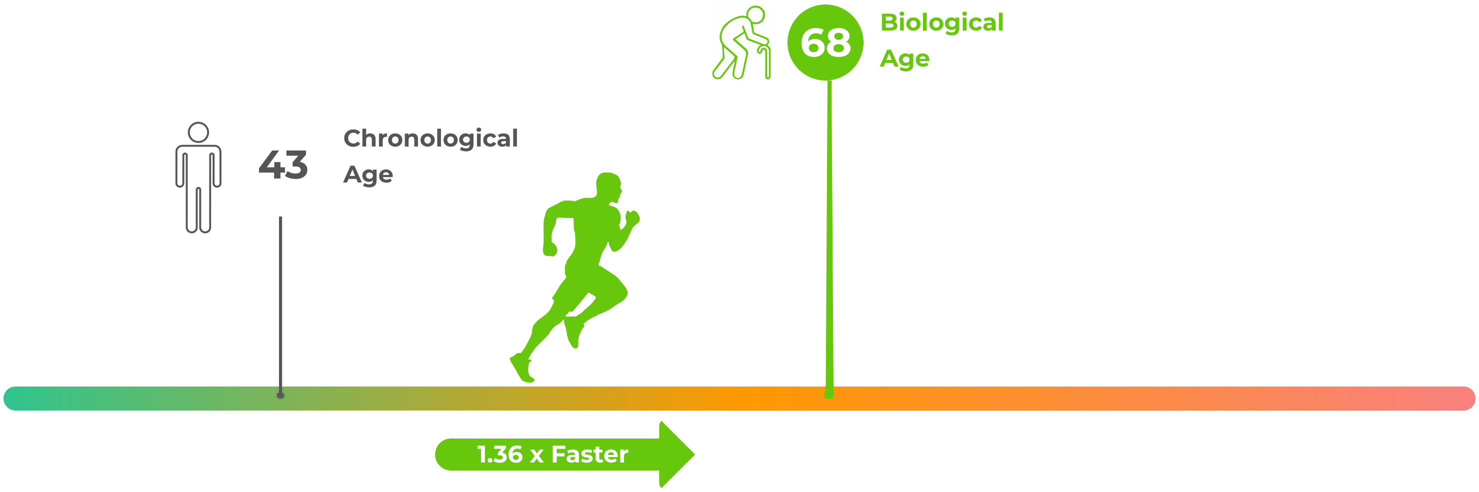
This metric assesses how the visual system — including the retina, lens, and optic nerve — is aging. The eye is sensitive to oxidative stress and often reflects early systemic decline. Methylation in genes related to photoreceptors, inflammation, and macular health can reveal early visual aging, allowing for preventive strategies against conditions like AMD and cataracts.



Immune System Integrity Age

Immune system integrity age reflects how well the innate and adaptive systems are functioning. Methylation in genes controlling cytokines, T-cells, and inflammation offers insight into immune resilience or decline. This helps predict vulnerability to infections, chronic disease, or cancer and guides personalized strategies to combat immunosenescence and inflammaging.

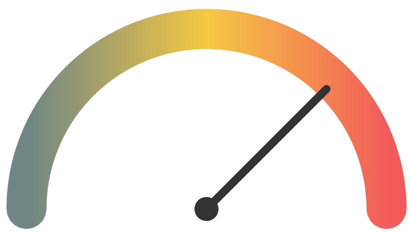
Chronological Age vs Biological Age



Your Biological Age is

HIGHER THAN

Your Chronological Age by **25** years.



68

Years Old

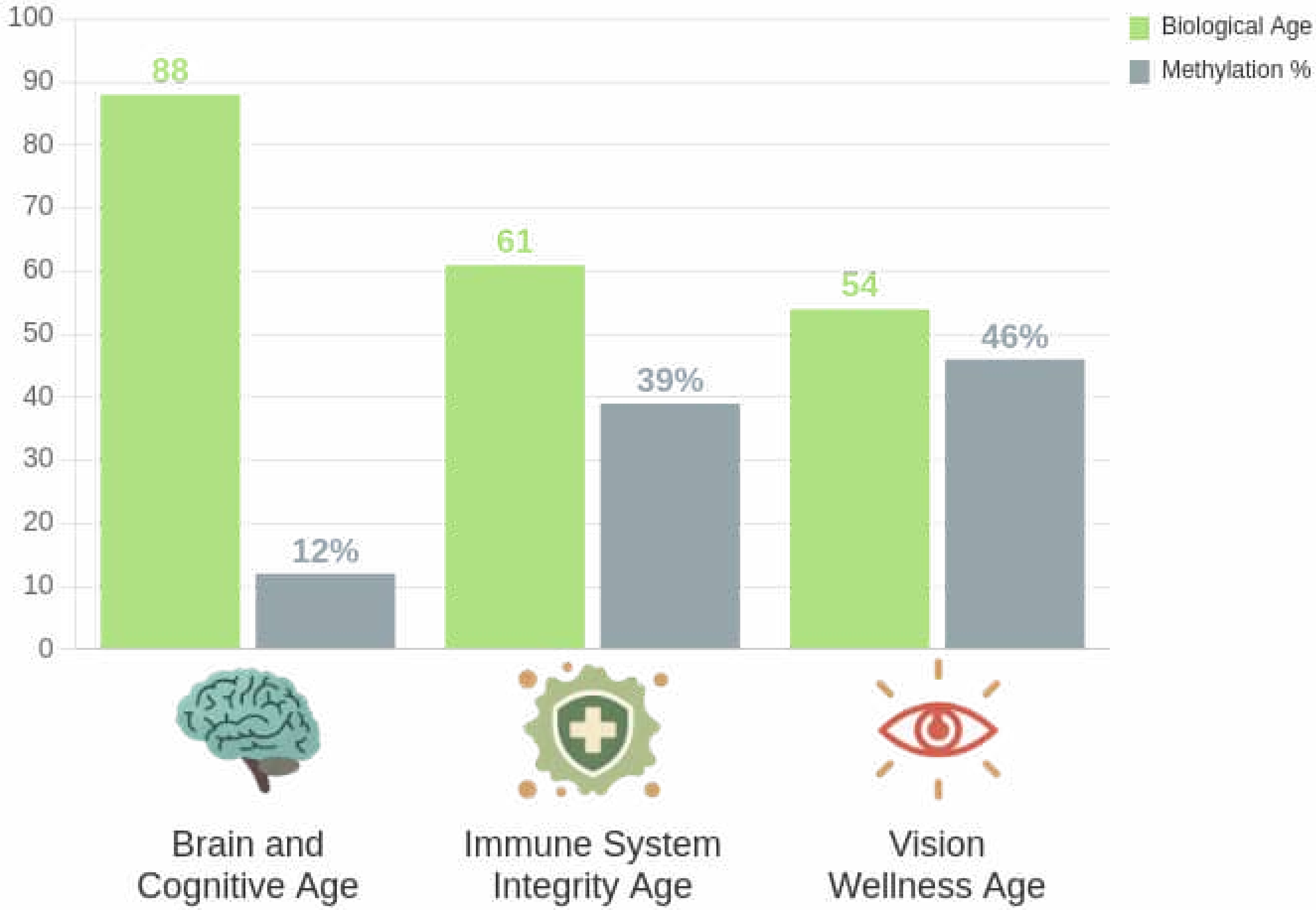
Your results show Accelerated Aging

You are aging **1.36 times** faster than your chronological age. In this case, the biological age is showing up older than the actual age. This may be a sign that certain systems in the body like brain function, vision, or immune integrity health are aging faster than expected. This could be influenced by genetics, chronic stress, inflammation, poor sleep, or lifestyle factors such as nutrition and physical activity. The good news is that these are often modifiable. Supporting the body with strategies like stress reduction, brain stimulation, anti-inflammatory nutrition, and immune-supportive therapies can help slow down this accelerated aging and get things back on track.

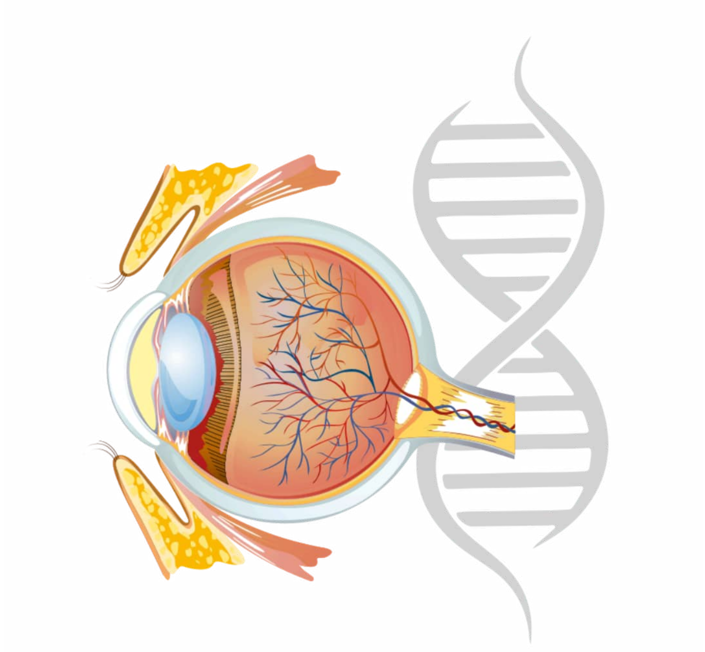
Chronological Age vs Biological Age

Your Chronological Age is **43**

Your Biological Age is **68**



Understanding Vision Wellness Aging Through Methylation



Vision aging is not simply a matter of declining eyesight, it reflects complex cellular and molecular changes occurring in the retina, retinal pigment epithelium (RPE), vasculature, and neural circuits of the visual system. Recent advances in epigenetics reveal that DNA methylation changes at specific CpG sites can significantly affect the expression of genes involved in retinal structure, oxidative defense, immune regulation, and neuroretinal signaling.

This section of the report analyzes an estimated 100 CpG methylation markers across genes critically involved in visual health and age-related macular degeneration (AMD). Genes like ENTPD1, DOT1L, and TRIM15 reflect the retina's inflammatory landscape, while others like NDUFS8, MPV17L2, and KEAP1 highlight the role of mitochondrial integrity and redox regulation in maintaining retinal resilience.

Methylation shifts in these genes may impair cellular functions such as:

- Photoreceptor and RPE homeostasis
- ATP production and mitochondrial signaling
- Vesicle transport and synaptic maintenance
- Immune activation and inflammatory resolution

Notably, the retina is highly susceptible to oxidative stress, and many genes covered here, such as KEAP1, S100A7, and NCF2, play frontline roles in defending against oxidative injury. Dysregulation of these pathways through aberrant DNA methylation may accelerate retinal aging and increase susceptibility to degenerative eye diseases.

By examining the methylation status of these vision-critical genes, we can better understand the biological aging process in the visual system, and guide interventions that support long-term retinal health, vascular integrity, and visual function.

Vision Wellness Epigenetic Result

Gene	% Methylation	Interpretation
APBA2	82.8%	Good Methylation
CHFR	78.2%	Good Methylation
DISP3	65.4%	Average Methylation
DLGAP2	76.5%	Good Methylation
DOT1L	84.5%	Good Methylation
ENTPD1	11.7%	Poor Methylation
GOLGA3	81.8%	Good Methylation
GPR146	37.3%	Average Methylation
HES6	2.7%	Poor Methylation
HTRA1	66.4%	Average Methylation
ILRUN	55.5%	Average Methylation
KCNQ1	50.3%	Average Methylation
KEAP1	12%	Poor Methylation
KPNB1	1.6%	Poor Methylation
LMAN2L	4.7%	Poor Methylation
MPV17L2	0.8%	Poor Methylation
NCF2	11.1%	Poor Methylation
NDUFS8	6%	Poor Methylation
PEX14	67.5%	Average Methylation
PTPRN2	82.8%	Good Methylation
S100A7	73%	Good Methylation
SAP130	3.2%	Poor Methylation
TMEM211	89.6%	Good Methylation
TOP2A	2%	Poor Methylation
TRIM15	86.1%	Good Methylation
TRIM26	49.6%	Average Methylation
UHRF1BP1	69.3%	Average Methylation

- Poor Methylation
- Average Methylation
- Good Methylation

Vision Wellness Methylation Status

Your methylation status for Vision Wellness is **Average**

Average methylation suggests partial protection of ocular health. While baseline retinal and lens function remain intact, there may be gradual accumulation of oxidative stress and reduced efficiency of repair mechanisms in photoreceptor cells. Vascular supply to the retina may show early microchanges, increasing the risk of mild vision disturbances with age, especially under poor lifestyle or nutritional conditions.

Supports long-term eye health and resilience	Offers partial protection with potential risks	Increases risk of eye diseases and aging
Good Methylation	Average Methylation	Poor Methylation

Genes Related to Vision Wellness Age

APBA2 is essential for neural communication and synaptic stability, supporting memory and protecting brain and retinal functions. Hypomethylation can enhance its expression, potentially improving neuronal resilience, while hypermethylation may reduce its function and contribute to neurodegenerative issues.

CHFR is a gene that regulates the cell cycle and maintains chromosomal stability, particularly in response to DNA damage, in retinal tissue. Hypomethylation can lead to excessive activation of CHFR, while hypermethylation may result in its silencing, both of which can impair the retina's capacity to handle genomic stress and affect age-related macular degeneration.

DISP3 (Dispatched RND Transporter Family Member 3) is essential for the Hedgehog signaling pathway, facilitating accurate signal delivery critical for retinal morphogenesis and development. Hypomethylation can lead to overactivation, while hypermethylation causes silencing of DISP3, both potentially disrupting normal retinal cell development and increasing vulnerability to age-related macular degeneration (AMD).

DLGAP2 is a synaptic scaffolding protein that supports neuronal signaling and synaptic plasticity, playing a critical role in retinal neuron communication. Hypomethylation may enhance retinal signaling efficiency, while hypermethylation could impair it, potentially increasing the risk of visual processing issues and degeneration, such as in age-related macular degeneration (AMD).

DOT1L regulates gene expression through histone methylation, supporting DNA repair and retinal cell function. Hypomethylation may weaken repair responses and increase vulnerability to stress in the retina.

Genes Related to Vision Wellness Age

ENTPD1 helps regulate purinergic signaling and immune responses by breaking down extracellular ATP and ADP into AMP. Hypomethylation may increase immune sensitivity and inflammation, especially in the retina.

GOLGA3 is a structural protein crucial for the Golgi apparatus and is involved in protein trafficking and cellular organization in retinal cells. Hypomethylation can enhance its expression, potentially improving protein transport and visual function, while hypermethylation may reduce its expression, negatively affecting these processes.

GPR146 is a G protein-coupled receptor involved in cell signaling and lipid regulation, contributing to retinal health and potentially preventing age-related macular degeneration. Hypomethylation of GPR146 may enhance its expression, while hypermethylation could suppress its function, impacting cholesterol metabolism and retinal vascular integrity.

HES6 is a transcription factor crucial for the development and maintenance of the nervous system, particularly in neuronal differentiation and retinal health. Hypomethylation may enhance HES6 activity, potentially improving cellular responses to stress, while hypermethylation could inhibit its function, leading to impaired neuronal adaptability and degeneration.

HTRA1 is crucial for protein quality control, extracellular matrix remodeling, and cellular stress responses, particularly in retinal and choroidal tissues. Methylation changes near HTRA1 can lead to hypo- or hypermethylation effects that alter retinal cell responses to damage, inflammation, and aging, impacting vision health.

Genes Related to Vision Wellness Age

ILRUN is a regulatory gene that modulates inflammatory signaling and lipid metabolism, crucial for maintaining retinal health. Hypomethylation of ILRUN may enhance inflammatory responses, while hypermethylation can suppress its activity, potentially impacting chronic inflammation and contributing to age-related macular degeneration (AMD).

KCNQ1 encodes a potassium ion channel essential for regulating electrical activity in tissues like the heart and pancreas, and it also contributes to retinal neuron function and visual processing. Hypomethylation of KCNQ1 can enhance its expression, potentially disrupting ion balance and excitability, while hypermethylation may reduce its expression, affecting visual performance and the eye's resilience to stress.

KEAP1 regulates the cellular antioxidant defense system by interacting with NRF2 to protect cells from oxidative stress, particularly in the retina. Hypomethylation of KEAP1 may enhance its expression, leading to increased detoxification of reactive oxygen species, while hypermethylation could reduce its function and compromise cellular resilience to stress.

KPNB1 is a transport protein that facilitates the movement of molecules between the nucleus and cytoplasm, regulating gene expression, stress responses, and cell cycle control particularly in metabolically active tissues like the retina. Hypomethylation can lead to increased gene expression and impaired stress responses, while hypermethylation may cause decreased expression and disrupted cellular functions, impacting the retina's ability to cope with environmental stressors.

LMAN2L encodes a protein essential for glycoprotein transport and processing in the endoplasmic reticulum and Golgi apparatus, impacting cellular stress handling and protein folding. Hypomethylation can increase its expression, potentially exacerbating stress responses in retinal cells, whereas hypermethylation may reduce its function, leading to impaired protein quality management.

Genes Related to Vision Wellness Age

MPV17L2 encodes a mitochondrial protein crucial for maintaining energy production and stability, particularly in high-energy tissues like the retina. Hypomethylation may lead to overexpression and potentially disrupt mitochondrial function, while hypermethylation can silence the gene, impairing mitochondrial health and contributing to retinal degeneration.

NCF2 is a subunit of NADPH oxidase that helps generate reactive oxygen species (ROS) for immune defense. Hypomethylation may enhance ROS activity, increasing oxidative stress in retinal tissues.

NDUFS8 is a key component of mitochondrial complex I, crucial for ATP production through oxidative phosphorylation, particularly in energy-demanding tissues like the retina. Hypomethylation of NDUFS8 can enhance its expression leading to hyperactive energy production, while hypermethylation may reduce its expression, potentially impairing energy efficiency and responsiveness to metabolic stress.

PEX14 is crucial for the assembly and function of peroxisomes, aiding in the detoxification of reactive oxygen species and lipid metabolism, particularly in retinal cells. Hypomethylation of PEX14 can enhance oxidative stress resilience in the retina, while hypermethylation may increase the risk of age-related macular degeneration (AMD).

PTPRN2 is crucial for neuronal development, insulin signaling, and neurotransmitter release, supporting neural communication and metabolic regulation in the brain and retina. Hypomethylation may lead to overexpression and exacerbate neurodegenerative conditions, while hypermethylation can reduce its expression, disrupting retinal neuron stability and visual signal integrity.

Genes Related to Vision Wellness Age

S100A7 is a protein that plays a crucial role in immune defense, inflammation, and maintaining epithelial barrier function, particularly in stress-exposed tissues like the skin and eyes. Hypermethylation of the S100A7 gene can lead to reduced expression, potentially exacerbating chronic inflammation and oxidative stress, while hypomethylation may enhance its activity, affecting ocular health.

SAP130 is a regulatory protein that controls gene expression, chromatin remodeling, and cell survival, particularly in response to stress and inflammation. Hypomethylation can lead to increased gene expression, while hypermethylation often results in decreased gene activity, which may disrupt cellular stress responses in retinal cells.

TMEM211 is a transmembrane protein implicated in cell signaling and development, particularly in sensory and epithelial tissues. Hypomethylation may enhance its expression and function, while hypermethylation could suppress its activity, affecting cellular communication and tissue integrity.

TOP2A is essential for maintaining DNA structure and stability, aiding in DNA unwinding, re-coiling during cell division, and proper chromosome separation and repair. Hypomethylation can lead to increased gene expression and potential dysregulation, while hypermethylation often silences the gene, both of which may compromise retinal cell function and exacerbate degeneration.

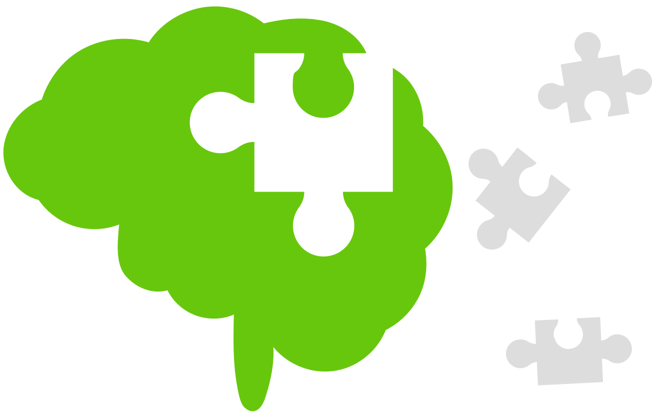
TRIM15 regulates immune signaling and stress responses, particularly in inflammation-prone tissues like the retina. Hypomethylation may increase immune activation and tissue sensitivity in the eye.

Genes Related to Vision Wellness Age

TRIM26 is a key protein in regulating innate immunity and antiviral defense, crucial for maintaining immune balance in the retina. Hypomethylation of TRIM26 can lead to increased immune responses and potential inflammation, while hypermethylation may dampen its protective effects and leave tissues vulnerable.

UHRF1BP1 is involved in epigenetic regulation and chromatin remodeling, influencing gene expression in response to cellular stress and maintaining retinal stability. Hypomethylation may lead to gene activation and inflammation, while hypermethylation can result in gene silencing and contribute to degenerative processes.

Understanding Brain and Cognitive Aging Through Methylation



Aging of the brain is a multifactorial process involving the gradual decline of synaptic integrity, neuroplasticity, neurotransmission, and neuroimmune balance. Emerging evidence shows that epigenetic changes, especially DNA methylation at CpG sites, play a pivotal role in modulating gene expression programs underlying cognitive function, neural maintenance, and neuroinflammation.

In this section, we examine 55 CpG sites across key genes implicated in synaptic function, neuronal development, neurotransmitter signaling, chromatin remodeling, and immune-neural crosstalk. Aberrant methylation patterns in these genes can influence the risk or trajectory of age-related cognitive decline, including memory loss, reduced processing speed, executive dysfunction, and increased susceptibility to neurodegenerative disorders.

Notable genes such as MDGA1, GRM7, MACROD2, and DNAJC6 regulate critical neuronal mechanisms like synapse formation, glutamatergic signaling, and vesicle recycling. Methylation shifts in ZNF238 and MSI2 impact neurogenesis and cortical structure, while LTBP3 and TNIP3 integrate immune and inflammatory pathways that affect neural resilience.

These methylation markers not only serve as early indicators of brain aging but may also offer actionable insights for lifestyle or therapeutic interventions aimed at preserving cognitive health across the lifespan.

Brain and Cognitive Epigenetic Result

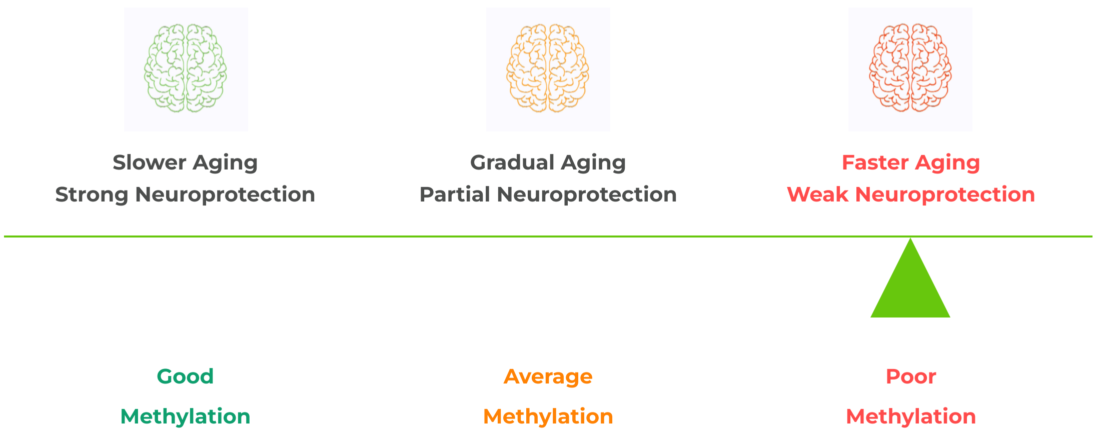
Gene	% Methylation	Interpretation
ABO	31.9%	Average Methylation
CD79B	21.8%	Poor Methylation
DAGLB	14.6%	Poor Methylation
DNAJC6	9.9%	Poor Methylation
GRM7	7.4%	Poor Methylation
KHDRBS2	10.3%	Poor Methylation
L3MBTL2	7.2%	Poor Methylation
LTBP3	9.7%	Poor Methylation
MACROD2	4.2%	Poor Methylation
MDGA1	38.3%	Average Methylation
MSI2	19.5%	Poor Methylation
RERE	6.4%	Poor Methylation
SPOCK2	16.7%	Poor Methylation
SSH2	12.5%	Poor Methylation
ST7	8.4%	Poor Methylation
TNIP3	3.9%	Poor Methylation
TRIP10	3.6%	Poor Methylation
ZNF238	8%	Poor Methylation
ZNF471	1.9%	Poor Methylation
ZSCAN1	7.4%	Poor Methylation

- Poor Methylation
- Average Methylation
- Good Methylation

Brain and Cognitive Methylation Status

Your methylation status for brain and cognitive is **Poor**

Unfavorable methylation patterns are linked to accelerated epigenetic aging in brain cells, impaired DNA repair, and dysregulated expression of genes involved in synaptic plasticity, detoxification, and inflammation control. This can heighten vulnerability to neurodegeneration, memory loss, and conditions like dementia or Parkinson’s disease.



Genes Related to Brain and Cognitive Age

ABO encodes glycosyltransferases that determine blood group antigens and is linked to vascular function. Epigenetic variation in this gene may influence cerebrovascular integrity, thereby contributing to age-related cognitive decline and brain health.

CD79B is part of the B-cell receptor complex, and its peripheral methylation may signal immune activation. Neuroimmune interactions can affect neuroinflammation and contribute to cognitive aging.

DAGLB (Diacylglycerol Lipase Beta) is essential for the synthesis of 2-arachidonoylglycerol, an endocannabinoid involved in synaptic signaling and neuroprotection. Methylation changes may affect endocannabinoid tone and neural homeostasis.

DNAJC6 (Auxilin) plays a critical role in synaptic vesicle endocytosis. Mutations are linked to Parkinsonian syndromes, and methylation variation may contribute to synaptic maintenance deficits in aging.

GRM7 (Glutamate Metabotropic Receptor 7) modulates synaptic transmission and plasticity via the glutamatergic system. CpG site methylation could influence excitatory neurotransmission and cognitive performance.

KHDRBS2 is an RNA-binding protein implicated in alternative splicing and mRNA regulation in neurons. Epigenetic variation may influence neuronal transcriptome dynamics critical to aging-related brain function.

Genes Related to Brain and Cognitive Age

L3MBTL2 encodes a chromatin-associated transcriptional repressor involved in cell cycle regulation and neural stem cell maintenance. Aberrant methylation may influence neurogenesis and epigenetic programming in brain aging.

LTBP3 (Latent Transforming Growth Factor Beta Binding Protein 3) regulates TGF-β signaling, which plays key roles in neurodevelopment, synaptic plasticity, and neuroinflammation. Methylation shifts may disrupt brain homeostasis.

MACROD2 is involved in chromatin remodeling and DNA repair. It has been associated with neuropsychiatric traits and its epigenetic modulation may influence brain aging and genomic stability.

MDGA1 (MAM Domain Containing Glycosylphosphatidylinositol Anchor 1) plays a critical role in synaptic development and neuronal cell adhesion, particularly in regulating inhibitory synapse formation. DNA methylation changes at CpG sites within this gene may alter synaptic architecture and connectivity, thereby influencing cognitive function and brain aging.

MSI2 (Musashi RNA Binding Protein 2) regulates stem cell fate and neurogenesis. Altered methylation patterns may affect the regenerative capacity of neural tissues during aging.

RERE (Arginine-Glutamic Acid Dipeptide Repeats) is a transcriptional coregulator essential for neural patterning and brain development. CpG methylation may modulate its expression, impacting structural and functional integrity in the aging brain.

Genes Related to Brain and Cognitive Age

SPOCK2 encodes a matricellular proteoglycan involved in maintaining extracellular matrix stability and synaptic structure. Changes in its methylation status may impact neuroplasticity and aging-related cognitive processes.

SSH2 encodes a phosphatase that regulates actin cytoskeleton dynamics, which are essential for synaptic morphology and plasticity. Methylation shifts may impair neuronal connectivity and adaptability.

ST7 (Suppression of Tumorigenicity 7) functions in signal transduction and gene regulation. Although its precise neurological role is unclear, methylation may reflect regulatory changes relevant to brain aging and resilience.

TNIP3 regulates NF-κB signaling and immune responses. Its methylation may be a marker of systemic inflammation, which is increasingly recognized as a contributor to neurodegeneration and brain aging.

TRIP10 (Thyroid Hormone Receptor Interactor 10) is involved in actin cytoskeleton organization and receptor internalization. Methylation may alter neuronal signaling pathways relevant to synaptic function.

ZNF238 , also known as RP58, is a transcriptional repressor involved in neurogenesis and cortical neuron differentiation. Its methylation has been linked to memory performance and structural brain differences.

Genes Related to Brain and Cognitive Age

ZNF471 is a KRAB zinc-finger transcriptional repressor. While its role in brain function is not fully characterized, altered methylation may influence gene regulatory mechanisms related to cognitive aging.

ZSCAN1 is a zinc-finger transcription factor whose methylation may influence neural gene regulatory networks. Though its neurological roles are still under study, CpG variation may relate to aging-related expression shifts.

Understanding Immune System Integrity Aging Through Methylation

As we age, the immune system undergoes a gradual functional decline, a process known as immunosenescence, marked by increased susceptibility to infections, chronic low-grade inflammation (inflammaging), and a diminished response to stress, vaccines, and injury. DNA methylation at specific CpG sites offers a powerful window into these underlying molecular shifts, serving as both biomarkers and modulators of immune aging.

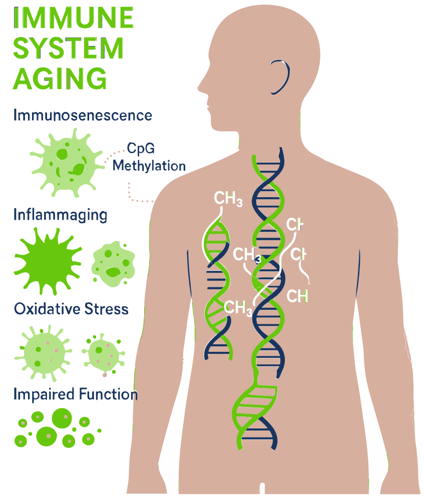
This section evaluates key immune-related genes [81 CpG sites] where age-associated methylation changes may influence processes like inflammatory signaling, oxidative stress response, DNA repair, and cell-mediated immunity. The panel includes genes such as:

IL6 and ENTPD1, which are central regulators of cytokine signaling and immune tolerance. GPX4, ELOVL2, and APOL3, which link oxidative stress resistance to immune cell integrity.

NOD2, SERPING1, and PSTPIP1, involved in innate immunity, complement regulation, and inflammasome activity

KDM4C, CHFR, and PRDM16, which regulate chromatin and transcriptional responses to immune stress.

ZIC4, IRX1, and MIR148A, highlighting immune-neural crosstalk and regulatory microRNA influence.



Epigenetic dysregulation in these genes may:

- Disrupt anti-inflammatory homeostasis
- Promote chronic immune activation
- Impair antigen presentation or phagocytosis
- Reduce genomic stability of immune cells

These methylation shifts are not uniform. While hypermethylation may suppress critical defense pathways, hypomethylation can lead to aberrant gene activation or genomic instability, both contributing to immunological drift and inflammatory diseases with age.

By integrating CpG methylation data across these 25 genes, this report highlights your immune aging trajectory, offering insights into potential vulnerabilities in inflammatory control, oxidative balance, and immune cell function, each vital for maintaining long-term systemic health.

Immune System Integrity Epigenetic Result

Gene	% Methylation	Interpretation
AHCYL2	11.3%	Poor
ANKRD11	44%	Average
APOL3	88.3%	Good
C1S	41.1%	Average
CHFR	88.8%	Good
ELOVL2	45.7%	Average
ENTPD1	49.5%	Average
ERCC1	2.5%	Poor
FAM38A	16.1%	Poor
GPX4	8.8%	Poor
GRIA2	13.1%	Poor
IL6	12.8%	Poor
IRX1	13.1%	Poor
KCNA4	5.2%	Poor
KDM4C	62.8%	Average
MAGI1	72.6%	Good
MIR148A	11.3%	Poor
NOD2	16.9%	Poor
NOS1AP	80.7%	Good
PRDM16	83.4%	Good
PSTPIP1	17.8%	Poor
SERPING1	86.9%	Good
SLC1A5	14.8%	Poor
WNT5B	67.8%	Average
ZIC4	13.1%	Poor

Poor Methylation
Average Methylation
Good Methylation

Immune System Integrity Methylation Status

Your methylation status for Immune System Integrity is **Average**

An average methylation profile indicates partially efficient immune regulation. While immune function remains adequate, gradual epigenetic drift may weaken T-cell diversity, slow immune cell regeneration, and impair rapid pathogen response. Low-grade chronic inflammation may start to appear, increasing long-term risk for inflammatory and autoimmune conditions.

Good Methylation	Average Methylation	Poor Methylation
Balanced immune cell development & controlled inflammatory responses	**Partially efficient immune regulation with gradual epigenetic drift**	Accelerated immune aging and excessive inflammatory gene activation

Genes related to Immune System Integrity Age

AHCYL2 regulates methionine metabolism and cellular methylation balance. Its dysfunction may lead to disrupted epigenetic regulation and contribute to metabolic decline with age.

ANKRD11 plays a role in chromatin remodeling and transcriptional regulation. Disruption of its function may contribute to epigenetic drift and altered gene expression with age.

APOL3 plays a role in lipid transport and innate immune modulation. With aging, its dysregulation may lead to increased lipid accumulation and inflammatory responses.

C1S is a component of the classical complement pathway in the immune system. Elevated levels in older adults contribute to chronic low-grade inflammation.

CHFR is a mitotic checkpoint gene involved in delaying cell division under stress. Age-related reductions in its activity can promote genomic instability and increase cancer susceptibility.

ELOVL2 is an enzyme involved in the elongation of very-long-chain fatty acids. Methylation of its promoter is one of the most robust biomarkers of biological aging.

ENTPD1 encodes an ectonucleotidase that regulates extracellular ATP and immune cell activation. Increased expression is associated with immune suppression and chronic inflammation in older individuals.

Genes related to Immune System Integrity Age

ERCC1 is crucial for DNA repair through the nucleotide excision pathway. Its age-related decline contributes to DNA damage accumulation and premature cellular aging.

FAM38A encodes a mechanosensitive ion channel that supports vascular tone and endothelial integrity. Altered function may impair tissue regeneration and contribute to vascular aging.

GPX4 is an antioxidant enzyme that protects lipids from oxidative damage. Its decreased activity with age contributes to oxidative stress and cellular degeneration.

GRIA2 encodes a subunit of AMPA-type glutamate receptors essential for synaptic transmission. Reduced GRIA2 expression is linked to cognitive decline and neural aging.

IL6 is a pro-inflammatory cytokine involved in immune signaling. Persistent elevation of IL6 is a hallmark of “inflammaging” and is associated with multiple age-related conditions.

IRX1 is a developmental transcription factor involved in tissue patterning. Its altered expression during aging may impair tissue repair and structural maintenance.

KCNA4 encodes a potassium channel important for regulating membrane excitability. Age-related changes in its function can impact neuronal signaling and cardiovascular performance.

Genes related to Immune System Integrity Age

KDM4C is a histone demethylase involved in epigenetic gene regulation. Its dysfunction can disturb chromatin architecture and accelerate cellular aging.

MAGI1 encodes a scaffold protein that maintains cell junction stability. Reduced expression with age may compromise epithelial barriers and promote inflammatory processes.

MIR148A is a microRNA involved in immune regulation and methylation control. Its dysregulation is linked to immune aging and altered epigenetic landscapes.

NOD2 is a pattern recognition receptor essential for innate immunity. Variants in this gene are associated with heightened inflammation and accelerated immune aging.

NOS1AP modulates nitric oxide signaling in neurons and blood vessels. Dysregulation may impair cognitive function and contribute to vascular aging.

PRDM16 controls mitochondrial biogenesis and brown adipose tissue development. Reduced activity with age can impair metabolic health and promote fat accumulation.

PSTPIP1 is involved in cytoskeletal dynamics and inflammatory signaling. Mutations or dysfunction may increase the risk of chronic inflammation and immune system deterioration with age.

Genes related to Immune System Integrity Age

SERPING1 encodes C1 inhibitor, which regulates the complement system. Alterations in this gene may drive immune system imbalance and chronic inflammation during aging.

SLC1A5 is an amino acid transporter essential for glutamine uptake and mTOR signaling. Impaired regulation of this pathway can accelerate aging by disrupting nutrient sensing and cellular metabolism.

WNT5B is part of the Wnt signaling pathway involved in cell proliferation and differentiation. Its dysregulation is linked to tissue fibrosis and diminished regenerative capacity with aging.

ZIC4 is a transcription factor critical for neural development and cerebellar function. Dysregulation of ZIC4 with age has been linked to increased risk of neurodegenerative diseases.

Age Optimization Framework | Lifestyle Insights

Vision Wellness

- Maintain optimal body composition – Aim for a waist-to-height ratio < 0.5 through strength training and anti-inflammatory movement (e.g., brisk walking, Pilates).
- Schedule annual dilated retinal exams with OCT imaging – Enables early detection of drusen, pigment changes, and microvascular alterations before symptoms arise.
- Eliminate smoking and reduce secondhand smoke exposure – Both deplete macular antioxidants (lutein, zeaxanthin) and constrict retinal vessels, accelerating AMD progression.

Brain and Cognitive Health

- Meditation (mindfulness/focused-attention) - Reduces stress, improves attention, thickens prefrontal cortex with regular practice.
- Dual-Task Training (e.g., walking while solving puzzles) - Boosts attention and multitasking ability.
- Maintain a regular circadian rhythm and sleep-wake cycle – Disruption is linked to increased Alzheimer's pathology.
- Manage chronic stress and reduce cortisol – Chronic stress impairs the hippocampus and executive function.

Age Optimization Framework | Lifestyle Insights

Immune Health

- Engage in resistance training – Builds muscle mass and improves myokine release, which has anti-inflammatory effects.
- Include regular nature exposure (forest bathing, green spaces) – Associated with reduced cortisol and pro-inflammatory cytokines.
- Practice intermittent fasting (as tolerated) – May enhance autophagy and regulate immune homeostasis.

Age Optimization Framework | Nutrition Insights

Vision Wellness

- Include foods rich in quercetin (apples, onions, tea)– Flavonoid with anti-inflammatory and antioxidant properties, protective for retinal health.
- Consume foods rich in lutein and zeaxanthin levels - such as eggs and a variety of fruits and vegetables, especially green leafy vegetables, including kale, spinach, broccoli and parsley.
- Include foods rich in resveratrol (e.g., red wine in moderation, grapes, cocoa)– Anti-angiogenic and antioxidant; may protect against AMD.
- Choose whole grains, legumes, and fiber-rich foods with low GI– Supports glycemic control, which is protective against diabetic retinopathy.

Age Optimization Framework | Nutrition Insights

Brain and Cognitive Health

- Black Coffee or green tea – Contain caffeine and polyphenols (EGCG, chlorogenic acid); enhance attention and cognitive longevity.
- Marine seaweed (e.g., kelp, wakame, nori) –Supplies iodine and polyphenols, balances neurotransmitters and reduces oxidative stress.
- Ground flaxseeds – Rich in ALA, lignans, and fiber, support anti-inflammatory action and brain protection.
- Turmeric with black pepper (curcumin + piperine) – Inhibit amyloid plaque buildup and improve mood and memory.
- Limit excess saturated fat from processed meats and fried foods – Protect hippocampal function and insulin signaling in the brain.
- Almonds, leafy greens (magnesium) – Enhance synaptic plasticity and reduce age-related memory loss.
- Eggs, beef liver, legumes (B12 and folate) – Prevent brain atrophy and reduce homocysteine-related neurotoxicity.

Age Optimization Framework | Nutrition Insights

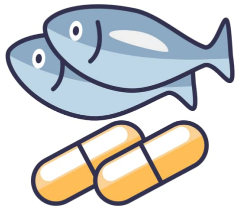
Immune Health

- Eat nuts and seeds(Almonds, walnuts, brazilnut, flaxseeds, pumpkin) regularly for vitamin E, magnesium, and healthy fats-supports immune signaling.
- Use extra virgin olive oil as a primary fat source-its anti-inflammatory and antioxidant properties.
- Incorporate dark chocolate (in moderation) for flavonoids- enhances T-cell and NK cell activity.
- Drink green tea daily for catechins like EGCG- support immune memory and reduce inflammation.
- Incorporate prebiotic fiber-rich foods, Leeks, asparagus, and chicory root feed-beneficial gut bacteria and promote production of SCFAs, which support immune and gut barrier health.
- Consume vitamin D-rich foods (fatty fish, egg yolks, mushrooms) or supplement to support T-cell activation and reduce respiratory infection risk.
- Incorporate carotenoid-rich foods (carrots, sweet potatoes, pumpkin)- supports mucosal immunity and antioxidant status.
- Eat foods rich in resveratrol (grapes, red wine in moderation)- its potential role in extending immune cell lifespan.

Age Optimization Framework | Supplement Insights

Vision Wellness

- Berberine
- Bilberry
- Grape seed extract
- ALA
- Vitamin B6 and Folate
- Lutein and zeaxanthin
- Zinc Sulphate
- Saffron
- Ginkgo biloba
- Curcumin
- Probiotics
  (Please consult a healthcare professional or your physician before starting any supplements.)



Brain and Cognitive Health

- Omega 3 Fatty Acids (EPA/DHA)
- Curcumin
- Vitamin D3+K2
- Methyl B12
- Methyl folate
- CoQ10
- Ashwagandha (Withania somnifera)
- Gotu Kola (Centella asiatica)
- Saffron (Crocus sativus)
  (Please consult a healthcare professional or your physician before starting any supplements.)

Age Optimization Framework | Supplement Insights

Immune Health

- Omega-3
- Zinc
- B12+Folate
- Melatonin
- NAC
- Vitamin D
- Probiotics
- Curcumin
  (Please consult a healthcare professional or your physician before starting any supplements.)

Age Optimization Framework | Labs Insights

Vision Wellness

- Reactive Oxygen Species (ROS)
- Vitamin D
- VCAM-1 and ICAM-1

Brain and Cognitive Health

- Plasma Neurofilament Light Chain (NfL)
- Plasma and CSF Amyloid-β & Tau
- BDNF / NfL Ratio
- hs-CRP
- IL-6
- Homocysteine
- GFAP (Glial Fibrillary Acidic Protein)
- Tumor Necrosis Factor-alpha (TNF-α)

Age Optimization Framework | Labs Insights

Immune Health

- Vitamin D
- Glucose profile
- TNF-α
- IL-6
- CBC
- Telomere length testing
- Hs-CRP

Citations

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Explanation Video

https://vimeo.com/1117375262

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Disclaimer

This epigenetic health report is intended exclusively for use by qualified healthcare professionals and is provided for informational, educational, and research purposes only. It is not intended to serve as a clinical diagnostic tool or to replace standard medical evaluations, testing, or judgment.

The interpretations presented are based on DNA methylation patterns and genetic variants associated with biological processes including, but not limited to, aging, pigmentation, immune response, and cellular resilience. These insights are generated through computational bioinformatic models informed by peer-reviewed scientific literature.

It is important to note that epigenetic markers are influenced by multiple variables beyond inherited genetics—such as tissue specificity, environmental exposures, ethnicity, lifestyle factors, and technical variability in sample collection and analysis. Accordingly, the findings in this report should be interpreted as part of a broader clinical and phenotypic context and not in isolation.

This report has not been reviewed or approved by regulatory agencies such as the U.S. Food and Drug Administration (FDA) and is not intended to guide or dictate treatment decisions. Clinical use of these insights remains exploratory and should be applied judiciously, in combination with standard diagnostic and therapeutic frameworks.

By reviewing this report, clinicians acknowledge its investigational nature and accept responsibility for integrating its findings into patient care using their own clinical expertise and discretion.