Reveal Your Biological Age

a personalized report based on your DNAge® results



Joe Doe

Test: myDNAge® | Sample ID: BL745554

Collection Date: May 2, 2021

Report Date: Jun 8, 2021

myDNAge®

Table of Contents

RESULTS

DNAge® Results 1-3

Epi-Metabolic Index Results 3

Genetic Variants Results 4

DNAGE DATA INTERPRETATION

The Science Behind DNAge® 5-6

Understanding DNAge® Results 7

DNAge® Improvement Plan 8-9

Epi-METABOLIC INDEX DATA INTERPRETATION

The Science Behind *Epi*-Metabolic Index 10

Understanding the *Epi*-Metabolic Index 11

Epi-Metabolic Index Improvement Plan 12-14

Overview of *Epi*-Metabolic Genes 15-18

GENETIC VARIANTS DATA INTERPRETATION

What is APOE? 19-20

What is MTHFR? 21

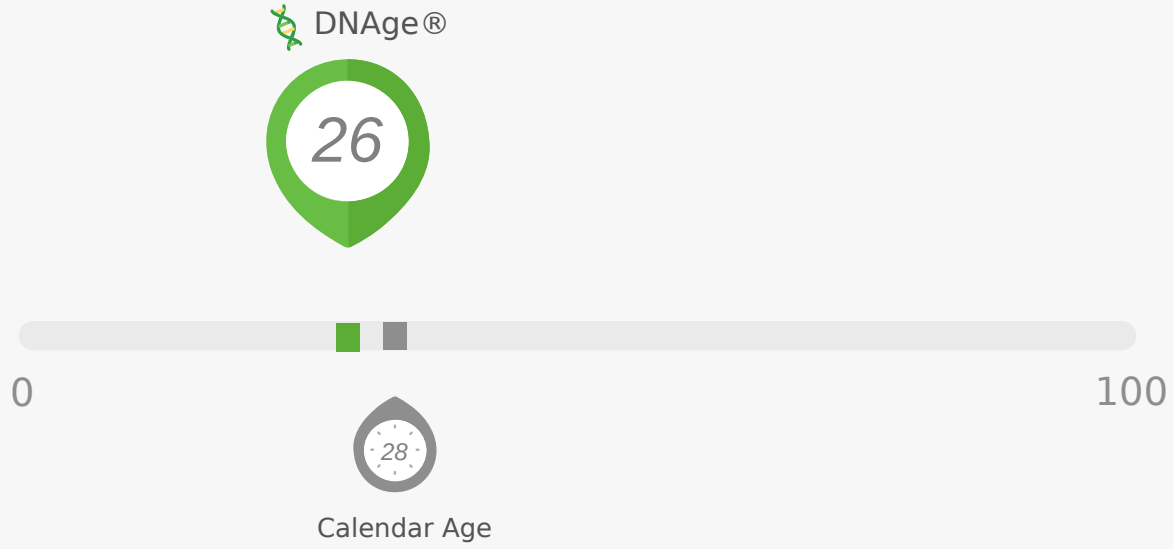
RESOURCES

References 22-27

Your DNAge Report

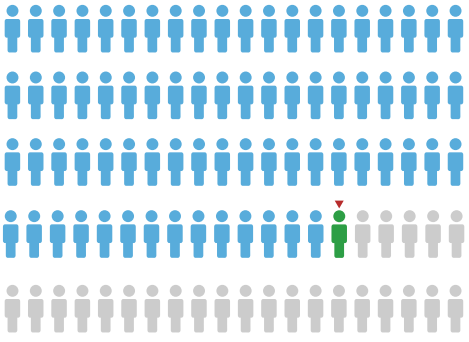
Your DNAge Result

Based on the methylation value of your sample, your DNAge is *26*.



DNAge Index

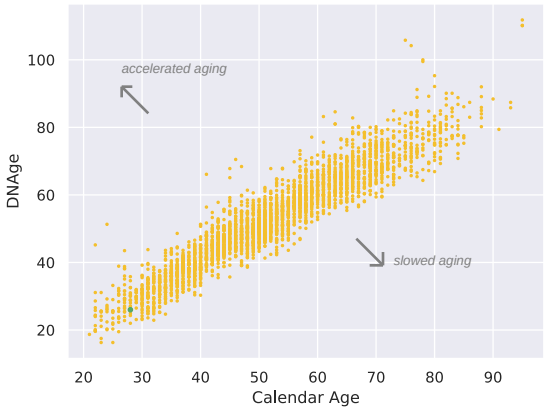
Your DNAge Index shows you are at *75th* percentile of your age. This means **you are younger than *75%* of people at your age.**



Older than you at your age

Younger than you at your age

Your results compared to the general population



This graph depicts your DNAge as it compares to the population across all recorded chronological ages included in our database. This graph is calculated in real-time and is based on Epimorphy's database. It is subject to change as our database continues to grow.

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

Sex-Specific DNAge

You are at the *73rd* percentile of your age in your sex group.



This means you are younger than *73%* of people at your age within your sex demographic.

See page 7 to learn more about your sex-specific DNAge Index

Your Aging Rate

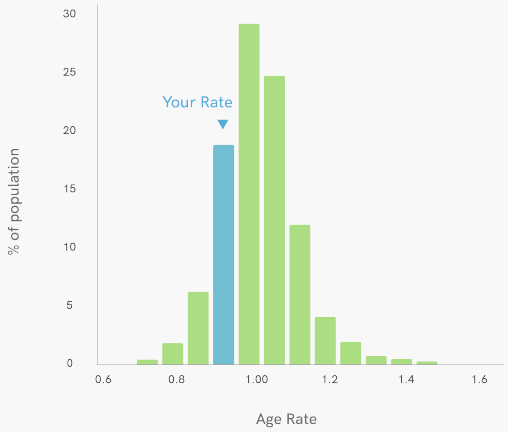
Based on your DNAge and calendar age, your age rate is:

0.93

Aging Rate Distribution

This graph depicts your aging rate as it compares to the population across every-one else in our data base.

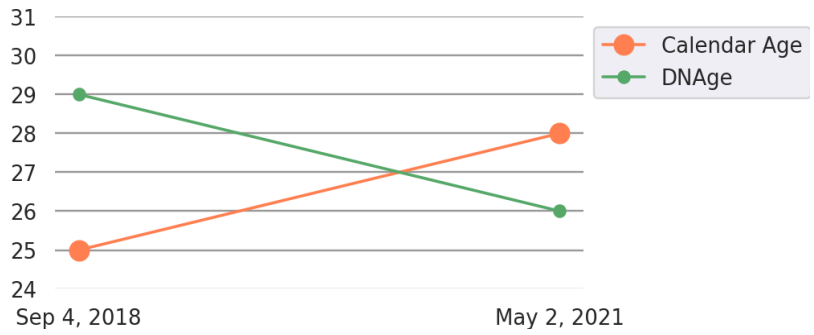
This graph is calculated in real-time and is subject to change as our database contin-ues to grow.



The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

Results Over Time

This is your DNAge pattern over time.



To monitor your DNAge changes, our scientific advisors recommend retesting 6-12 months after your original test.

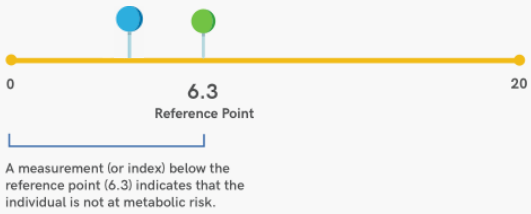
See page 5 to learn more about DNAge

Epi-Metabolic Index

A measurement based on DNA methylation loci that have been scientifically shown to be significantly associated with metabolic disorders.



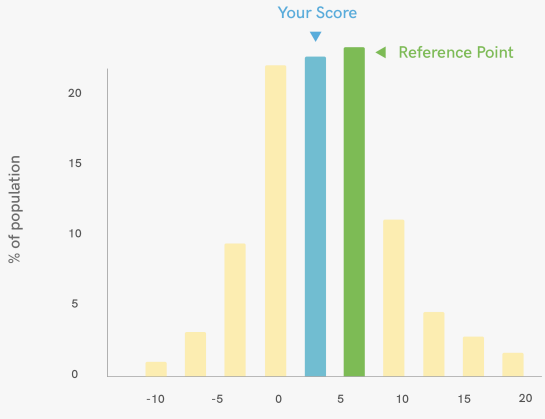
Your *Epi*-Metabolic Index



A measurement (or index) below the reference point (6.3) indicates that the individual is not at metabolic risk.

This graph highlights your *Epi*-Metabolic index as it compares to our population database.

See page 10 to learn more about the Epi-Metabolic index



The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

Genetic Variants Report

Genetic variation can occur in our genes and is referred to as a Single Nucleotide Polymorphisms (SNP). Here we report two sets of SNPs that may contribute to Aging and DNAge estimation.

APOE Gene

The APOE gene is involved in making a protein that helps carry cholesterol and other types of fat in the bloodstream. Certain genetic variants of the APOE gene on chromosome 19 are associated with reduced longevity and increased risk of Alzheimer's disease onset. Other genetic variants of APOE have been reported as promoting longevity.

Your Single Nucleotide Polymorphism (SNP) in the ApoE gene:



	Genetic Code
SNP 1 rs429358	T/T
SNP 2 rs7412	C/C

Common Name: E3/E3

There are three common allelic variants of ApoE as defined by two SNPs, known by the common names: E2, E3, and E4.

See page 19 to learn more about APOE

MTHFR Gene

The MTHFR gene encodes the vitamin-dependent enzyme, methylenetetrahydrofolate reductase. MTHFR converts dietary folic acid (Vitamin B9) from consumed food to methyl-folate - which plays a role in One-Carbon metabolism in your body - an essential metabolic pathway.

Your Single Nucleotide Polymorphism (SNP) in the MTHFR gene:



	Genetic Code
SNP 1 rs1801131	C/C
SNP 2 rs1801133	A/A

Within the MTHFR gene, there are two SNPs, 677C>T (rs1801133) and 1298A>C (rs1801131). Variations could potentially result in reduced enzymatic activity and, subsequently, impaired methylation in the human body.

See page 21 to learn more about MTHFR

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

The Science Behind DNAge®

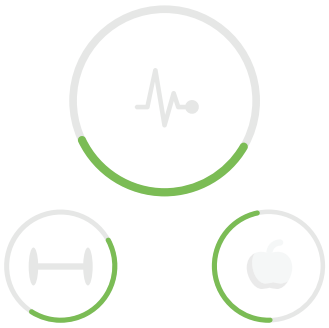
What is Epigenetics?

Epigenetics is a term from the field of biology. It refers to changes in gene expression that occur without altering a gene's primary DNA sequence. During development, epigenetic mechanisms turn genes on or off in a highly regulated manner to give and maintain identity to each cell. For example, each of your cells contains the exact same genetic sequence, yet somehow a liver cell must know it's a liver cell, a heart cell must know it's a heart cell, and so on. Thanks to epigenetics, you possess complex organ systems that carry out diverse functions necessary to sustain life.



Why is this Important?

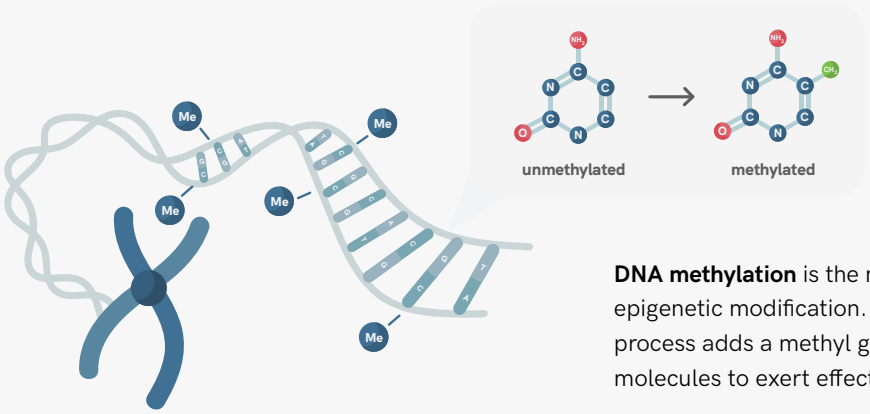
Epigenetic control of gene expression continues throughout our lives, and it is directly influenced in response to our continually changing external environment. Importantly, whereas the DNA sequences that make up our genes are static and do not change, over the course of our lives our epigenetics will change. Through years of scientific research we know that life-style factors including exercise, diet, stress, smoking, or alcohol consumption all influence epigenetic ability to control our genes' DNA. In that context, epigenetics really defines a process in which our own personal experience, or our own life history, is directly written onto our DNA.



Crucially, a consistently growing mountain of scientific evidence suggests that epigenetic mechanisms play a critical role in regulating human health including processes as diverse as growth and development in the early stages of life, everyday metabolism throughout your life, and in the progression of diseases such as cancer as we grow older. You can have tremendous influence over your epigenetics and thus how you age. You can have a positive impact by making healthy lifestyle choices, or a negative impact, as many unhealthy choices are correlated with higher rates of aging.

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

The Fifth Base



DNA methylation is the most well studied epigenetic modification. This biological process adds a methyl group (Me) to DNA molecules to exert effects on gene expression.

What is Biological Age?

Biological age is a concept that helps quantify how old the cells are in our body. It can be calculated based on various properties and biomarkers that correlate with aging and decline. Epigenetic biomarkers, such as DNA methylation, have been shown to accurately measure biological age.

Furthermore, recent studies have even demonstrated the detrimental impact that different diseases or syndromes have upon your biological age. UCLA professor Dr. Steve Horvath pioneered the field of DNA methylation-based biological age prediction to create an epigenetic aging clock known as Horvath's Clock, which uses 353 DNA sites where methylation can occur (commonly referred to as CpG sites). Horvath used the data from approximately 8000 human research subjects in a 2013 study that demonstrated a modern and accurate way to measure biological age. That study has since been cited over 1500 times and remains the standard for epigenetic measurements of biological age.



myDNAge

The MyDNAge® report holds an exclusive license to the original 353 CpG sites used in Horvath's Clock, and has since added an additional 2000 CpG sites to expand the capabilities and performance of the mathematical model used for measuring biological age. Taken together, the results have a strong correlation with chronological age and allows us to quantify the aging process.

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

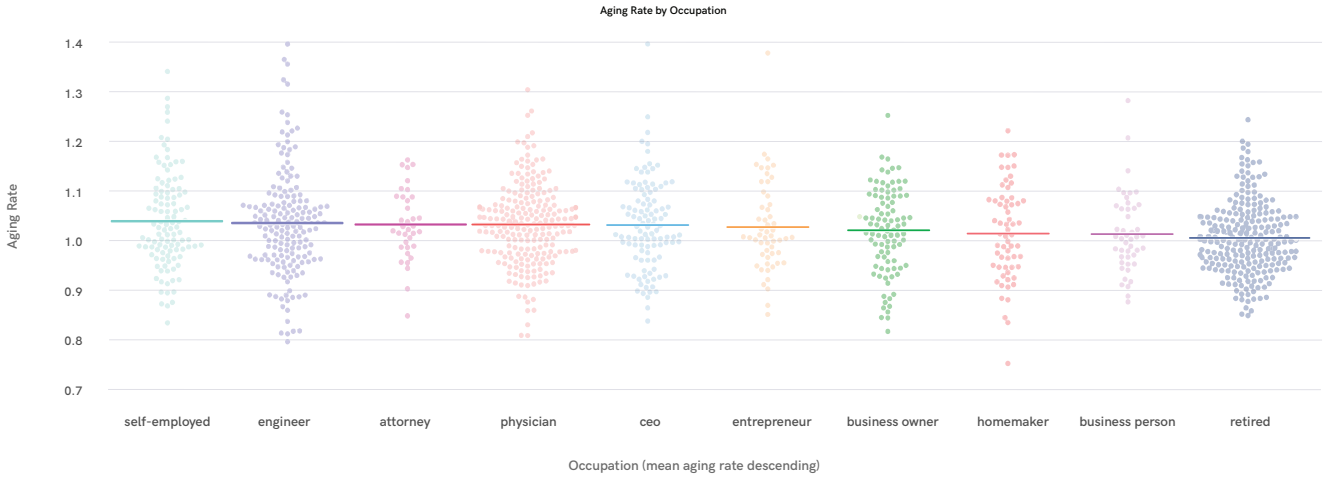
Understanding *my*DNAge® Results

Women exhibit lower epigenetic age rates than men.



A sex-specific biological age trend is shown above based on our database.

Occupation-derived stress impacts aging rate

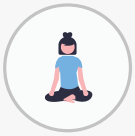


The graph above lists occupations with the average aging rate descending from left to right. Relatively higher stress occupations exhibit higher aging rate.

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

DNAge Improvement Plan

Reduce



Reduce chronic stress

Practice mindful stress-relieving methods such as meditation and yoga. This is an essential piece to improving DNAge, where research has proven that stress accelerates epigenetic aging.



Reduce exposure to tobacco

Research has shown the ample benefits of reduction in smoke exposure- including tobacco, and chronic exposure to wildfires. Benefits include reduction in cardiovasular risk factors, life expectancy and improvement in biological age.



Reduce exposure to chronic air pollution

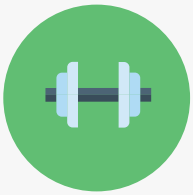
Long-term exposure to ambient air pollution is linked to a host of adverse age-related ourtcomes- including but not limited to casdiovascular disease, impaired cognitive function, cancer, metabolic outcomes, and mortality. All of the aforementioned air pollution associated outcomes are also associated with aging. Studies have explored the underlying biology of these associations and have linked air pollution exposure with epigenetic alterations.



Reduce exposure to environmental toxins

Environmental toxins include ionizing radiation and endocrine disruptors. Exposure to ionizing radiation produces oxygen-derived free radicals in human tissue. Whereas, endocrine disruprors (such as BPA and phthalates) are hormonally active agents/chemicals that can interfere with the natural cycle of hormones in the human body. When absorbed in the body, an endocrine disruptor can decrease or increase normal hormone levels, mimic the body's natural hormones, or alter the natural production of hormones. Endocrine disruptors are found in processed food, plastics, and cosmetics.

Improve



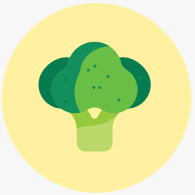
Exercise mindfully

Ample research has proven the benefits of daily exercise - advantages range from cardiovascular health and increased mobility to reduction of cancer risk. Too much exercise, however, can accelerate biological aging.



Get adequate sleep consistently

Cumulative evidence points to a role of sleep loss and sleep disturbances as a contributor to early disease onset and shortened survival.



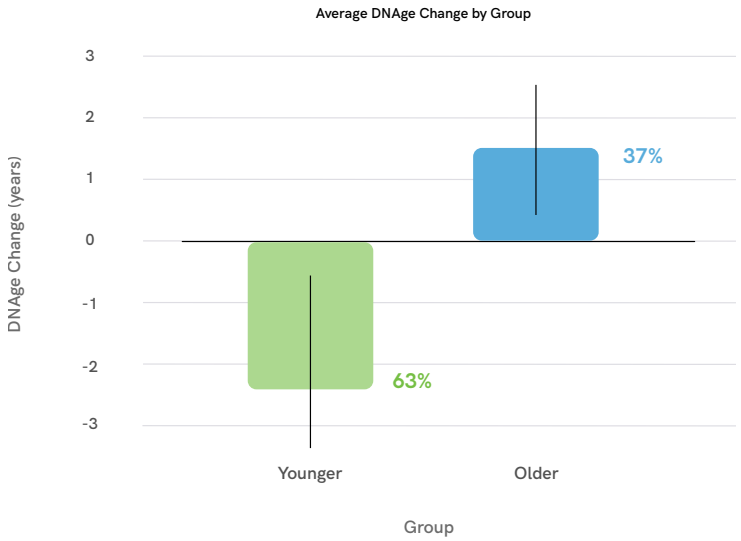
Consume organic food and minimize processed food and refined sugars

An organic, wholefood diet has been shown to not only maximize the antioxidant potential of our cells, but also eliminate harmful carcinogens and gerontotoxins (aging toxins) entering our boodstream.

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

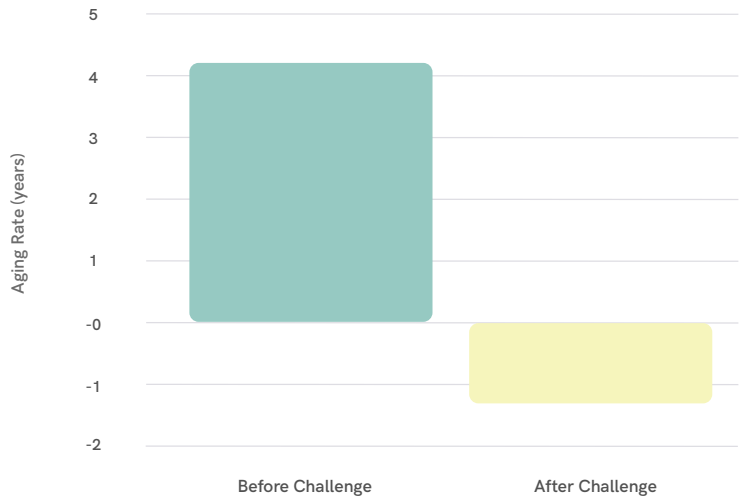
DNAge Can Be Improved With Good Practice

Epimorphy launched an annual New Year New Me global competition where participants competed against one another to adopt healthy lifestyle interventions to reduce their biological age.



The **New Year New Me** competition was extremely successful where 63% of participants were younger after they implemented healthy lifestyle interventions, positively extending their healthspan and quality of life.

It is worth noting that we focus on non-extreme interventions, meaning that relatively easily achievable changes in one's lifestyle beahviors lead to a significant slowing down of biological aging biomarkers, which in turn is associated with lower risk of developing age-related disease, and incresed quality of life in the older age.



The winner of last year's competition elected to practice a combination of several lifestyle changes throughout the 6-month timeframe, including walking 5-6 miles per day, a wholesome diet consisting of plenty of fruits, vegetables, fish, seafood, nuts, whole grain bread, limited cheese, yogurt, and sweets. The winner transitioned to a ketogenic diet with intermittent fasting, and also started drinking matcha tea and cocoa for nutritional benefits.

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

The Science Behind Epi-Metabolic Index

Rapidly accumulating experimental, clinical, and epidemiological evidence indicates that epigenetic factors, especially DNA methylation, are a key element underlying metabolic traits. DNA methylation is both static and dynamic, which can respond to cues from both external and internal environments. Environmental influences have been identified as major risk factors of metabolic disease. A growing body of clinical studies have identified methylation signatures associated with several cardiometabolic traits including BMI, blood pressure, and lipid levels. We utilized the scientifically proven DNA methylation signatures to build the Epi-Metabolic index.

A star system has been adopted to indicate scientific evidence for each of the analyzed DNA methylation sites.

Gene	Evidence Level
ABCG1	****
CPT1A	****
PHGDH	****
SREBF1	****
TXNIP	****
HIF3A	***
KLF13	***
MYO5C	***
SARS	***
SLC7A11	***
SOCS3	***
USP22	***

****	Strong scientific evidence. A well-powered study with over one thousand people, and another additional stud(ies) showing the same results.
***	Strong scientific evidence. A study with an approximate moderate sample size of 500 or more people, with or without a replicated study.
**	Potential scientific evidence. Multiple small sample size published studies with some consensus.
*	Unknown scientific significance.

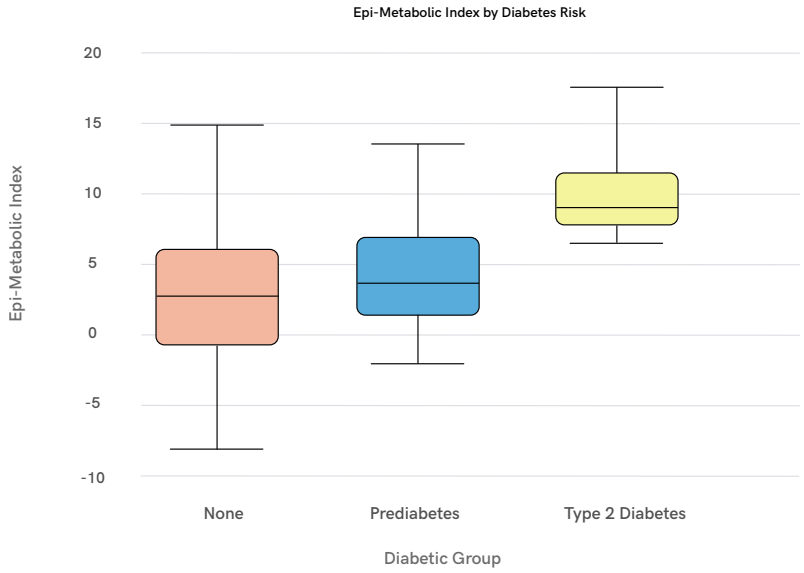
While we have much to learn, we know there are many genes that regulate metabolism, how your body handles nutrition intake and how food and nutrients optimize your gene expression.

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

Understanding Epi-Metabolic Index

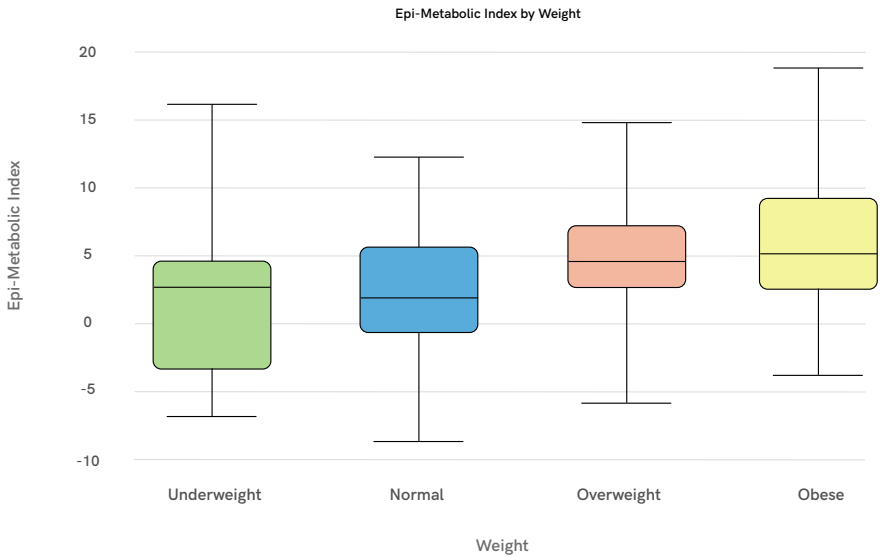
The Epi-Metabolic index test was developed to measure metabolic disorder susceptibility, a factor which affects overall biological age. In our database, 90% of subjects without a known metabolic disorder had an index below 6.3.

Diabetes



An increasing trend of Epi-Metabolic index for non-diabetes, prediabetes, and those diagnosed with Type 2 Diabetes is observed in our current population database.

Weight

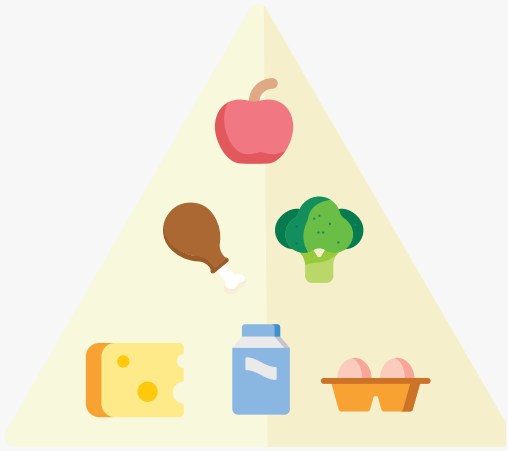


An increasing trend of Epi-Metabolic index from normal to obese is observed based on our current population database. Underweight individuals also demonstrate modest increase of Epi-Metabolic index.

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

Epi-Metabolic Index Improvement Plan

Nutrition



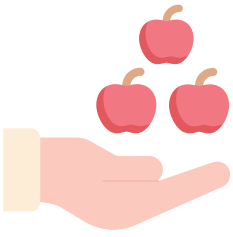
For decades, it has been apparent that nutrition modulates the aging process. The earliest unequivocal evidence for the impact of nutrition on aging came from studies in rodents showing that dietary restriction (energy restriction while ensuring adequate nutrient supply) increased both lifespan and reduced (or delayed) the development of age-related diseases.

Dietary restriction is now a very well-established experimental paradigm that extends health span in many species, including humans. A notable study showed that monkeys who underwent a 30% dietary restriction in adulthood were leaner and had a lower burden of age-related diseases. Additionally, a CALERIE (Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy) randomized trial indicated that slowed biological aging is observed in non-obese adults with prolonged caloric restriction.

Two factors come into play in nutrition:



Quality



Quantity

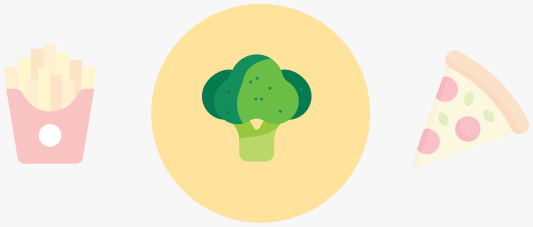
The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

Control the amount of food intake.



- Avoid overeating and binge eating.
- Intermittent fasting has emerged as a plan that focuses on when you eat as opposed to what you eat. This method requires alternate periods of extended fasting with relatively short windows of time during which food is consumed.
- Eat slowly and try not to perform other tasks while eating. Your brain will signal your satisfaction at the appropriate time when you are not distracted.
- Maintain a healthy weight for your height and age.
- Healthy weight loss is only accomplished by monitoring a consistent calorie deficit.

Be selective of the food you consume.



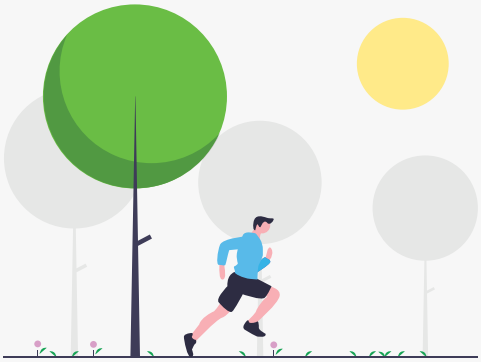
- Did nature make this or did man make this? Eat organic as often as you can. Adopt a diet based on the consumption of plant foods with a low glycemic load, low in saturated and trans-fat, and rich in antioxidants.
- Replacement of refined grains with whole grains.
- Increase daily consumption of vegetables and fruits with at least one portion of raw vegetables and one portion of cooked vegetables at each meal, and at least 2-3 portions of fruits.
- Focus on a Mediterranean diet.

  Mediterranean diet – a dietary pattern which is characterized by low intake of dairy foods, meats and meat products, moderate-to-high consumption of fish, high consumption of legumes, nuts, cereals, and exclusive use of extra-virgin olive oil as dressing and cooking fat.

- Avoid processed food and refined sugar. Cakes and desserts should be consumed no more than once weekly.
- When reaching for a snack, grab two handfuls of nuts a day. Nuts are great for your waistline, long-term health, and help prevent heart disease and diabetes.

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

Exercise.



- Move daily. Even on busy days, integrate a short 20-minute daily walk of moderate intensity.
- Avoid overexertion. Too much exercise can be as harmful as no exercise. Your best guide is how your body feels, so listen to your body.
- Build on your exercise regimen slowly.

Maintain a healthy weight.



- Both a healthy diet and exercise help attain and maintain a healthy weight.
- Caloric deficits are the only way to lose weight, when necessary. Energy output (Basal Metabolic Rate and calories burned in exercise) must exceed energy input (what we eat).
- When attempting to reach a heathy weight, maintain protein intake in your diet. Weight loss should be due to fat loss as opposed to muscle mass loss.

In the next eight pages, we provide gene function information for each gene included in the Epi-Metabolic index, and the impact of these genes on metabolic health. We also provide recommendations to maintain the integrity of each gene's methylation profile.

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

Epi-Metabolic Index

ABCG1 (ATP Binding Cassette Subfamily G Member 1)

Increasing evidence suggests that ABCG1 is involved in cholesterol metabolism and inflammatory stress in obesity-related disease risk. ABCG1 is highly expressed in adipose tissue and promotes the uptake of triglyceride into adipocytes. In liver and macrophages, it might play a regulating role of tissue lipid levels.

Extensive research has shown that DNA methylation at the ABCG1 site of our interest is positively correlated with:

- Obesity
- Fasting insulin
- Body mass index (BMI)
- Risk of type 2 diabetes (T2D)
- Triglyceride (TG) levels
- High-density lipoprotein (HDL) levels

CPT1A (Carnitine Palmitoyltransferase 1A)

CPT1A is one of the three isoforms of Carnitine palmitoyltransferase 1 (CPT1). CPT-1 is an important enzyme involved in the regulation of mitochondrial fatty acid oxidation (FAO). CPT1A is highly expressed in the liver, where it initiates its function and therefore helps regulate serum triglyceride levels.

More than 30 studies have shown that DNA Methylation at the CPT1A site of our interest is associated with:

- Lipid concentrations in ApoB lipoproteins
- Triglyceride (TG) levels
- Total serum Triglyceride (TG)
- Type 2 diabetes (T2D) / type 2 diabetes mellitus (T2DM)
- Hepatic fat
- Blood pressure traits

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

PHGDH (Phosphoglycerate Dehydrogenase)

PHGDH is the enzyme that catalyzes the first and rate-limiting step in the phosphorylated pathway of serine biosynthesis. Many studies warrant examination of this enzyme in metabolic and obesity-related phenotypes. The metabolic implications of PHGDH are further extended by evidence of its overexpression in some cancers, as it drives metabolic changes leading to rapid cellular growth.

Research shows that DNA methylation at the PHGDH sites of our interest is associated with:

- Triglyceride (TG) levels
- Polyunsaturated fatty acids (PUFAs) measures
- Obesity
- Nonalcoholic fatty liver disease (NAFLD)
- Systolic and diastolic blood pressure
- Body mass index (BMI) and waist circumference

SREBF1 (Sterol Regulatory Element Binding Transcription Factor 1)

SREBF1 binds a motif in the promoter region of the LDLR (Low density lipoprotein receptor gene) to activate its transcription for cholesterol metabolism. SREBF1 methylation may serve as a potential "multipurpose" biomarker for both lipids and cardiometabolic dysfunction.

Diverse cohorts have repeatedly found that DNA methylation at the SREBF1 sites of our interest is associated with:

- Fasting blood total cholesterol levels
- Liver triglyceride (TG) levels
- Body mass index (BMI)
- Type 2 diabetes (T2D)
- Monounsaturated fatty acid intake

The methylation profile of this gene could be used as an early biomarker of type 2 diabetes by determining early dysfunction in fatty acid metabolism.

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

TXNIP (Thioredoxin Interacting Protein)

TXNIP has emerged as a major factor regulating pancreatic beta cell dysfunction and death which are key processes in the pathogenesis of type 1 and type 2 diabetes. TXNIP might also contribute to nutrient sensing, energy metabolism, and regulation of cellular redox.

Several EWAS studies suggest, irrespective of ethnic and social differences, that DNA methylation at the TXNIP sites of our interest is associated with:

- Fasting glucose levels
- Hemoglobin A1c (HbA1c) levels
- Incident of type 2 diabetes (T2D)
- Insulin sensitivity

HIF3A (Hypoxia-Inducible Factor 3 Alpha)

HIF3A belongs to the transcription factor family of hypoxia-inducible factors (HIFs) which regulate the cellular response to hypoxia. HIF3A may also be involved in the regulation of glucose metabolism and to function as an accelerator of adipocyte differentiation.

The DNA methylation at the HIF3A sites of our interest have been reported to be associated with:

- Body mass index (BMI)
- Waist circumference
- Thickness of visceral adipose tissues

Myo5C (Myosin VC)

DNA methylation at MYO5C gene is a well-documented obesity associated marker. MYO5C is particularly abundant in epithelial and glandular tissues including in the pancreas, prostate. Methylation at MYO5C has been associated with serum C-reactive protein (CRP) levels which is an indicator of chronic low-grade inflammation.

The DNA methylation at the MYO5C sites of our interest have been reported to be associated with:

- Obesity
- Increase fasting glucose levels
- High density lipoprotein (HDL) levels
- Body mass index (BMI)
- Serum C-reactive protein (CRP)

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

SARS (Seryl-tRNA Synthetase)

SARS encodes for a protein that catalyzes the transfer of L-serine to tRNA for protein synthesis. Differential methylation of peripheral blood–derived DNA at our CpG site of interest has been associated with:

- Blood triglyceride (TG) levels
- Body mass index (BMI)
- Smoking
- All-cause mortality

SLC7A11 (Solute Carrier Family 7 Member 11)

SLC7A11 encodes for a cysteine-glutamate anti-porter regulating levels of the antioxidant glutathione, and it is a known target of the environmental neurotoxin β-methylamino-L-alanine (BMAA). Studies identify the SLC7A11 gene as a plausible biological target in Parkinson's disease.

The DNA methylation at the SLC7A11 sites of our interest have been reported to be associated with:

- Systolic and diastolic blood pressure
- Arteriosclerotic traits of kidney and heart
- Alcohol consumption

SOCS3 (Suppressor of Cytokine Signaling-3)

SOCS3 is a well characterized gene involved in immune system regulation, such as infection and autoimmunity. Habitual diet quality was associated with differential DNA methylation levels of SOCS3. Recently, it was reported that methylation of SOCS3 moderates the effect of cumulative stress on body weight.

The DNA methylation at the SOCS3 sites of our interest have been reported to be associated with:

- Obesity
- Multiple metabolic syndrome (MetS) traits
- Type 2 diabetes (T2D)
- Cumulative stress

USP22 (Ubiquitin-Specific Peptidase 22)

USP22 has been observed to mediate various cellular processes including cell proliferation and apoptosis (cell death). Aberrant expression of the USP22) has been associated with poor cancer prognosis and neurological disorders.

The DNA methylation at the USP22 sites of our interest have been reported to be associated with:

- Body mass index (BMI)
- Obesity

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

Single Nucleotide Polymorphism (SNP) Data

Genetic variation which can occur in our genes are referred to as a Single Nucleotide Polymorphisms (SNP). Each SNP represents a difference in a single DNA building block, called a nucleotide. Here we report two sets of SNPs that may contribute to Aging and DNAge prediction.

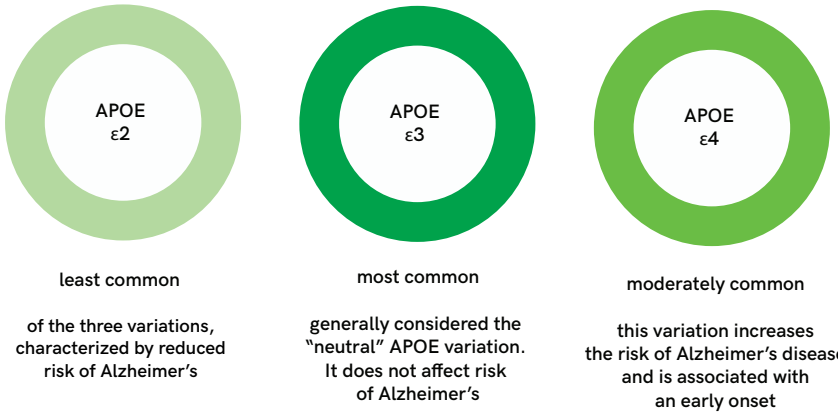
APOE

What is APOE?

APOE stands for **Apolipoprotein E** and is involved in the metabolism of fats in the human body. In the central nervous system, APOE is produced by astrocytes (a type of brain cell) and it is an essential cholesterol carrier in the human brain that transports cholesterol to neurons.

What are the APOE genetic variations -polymorphisms- of principal interest?

APOE is polymorphic with three major forms, namely ε2, ε3, ε4.



When approaching the concept of risk factors, it is essential to consider not only if the variants put an individual at risk for a condition, but if so, how much risk.

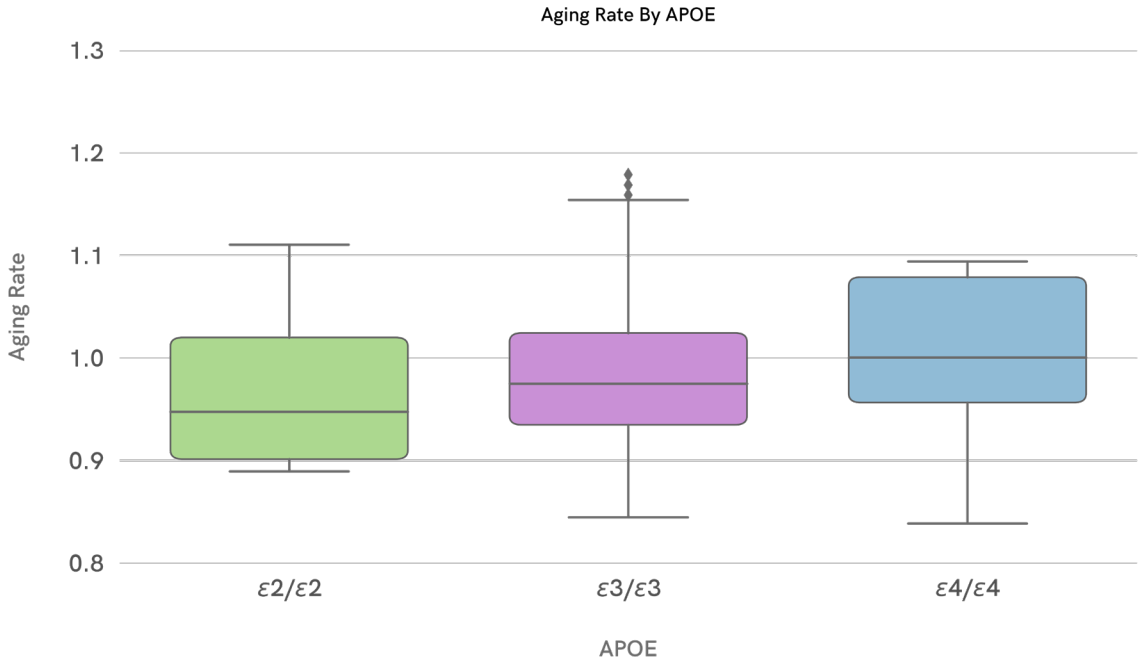
You inherit one APOE gene from each of your parents, for a total of two copies. Having one APOE ε4 gene increases your risk of developing Alzheimer's disease two- to three-fold. Having two APOE ε4 genes, significantly increases your risk by approximately eight- to twelve-fold.

It is important to note that not everyone who has one – or even two – APOE ε4 gene polymorphisms develops Alzheimer's disease. This genetic polymorphism is not a direct cause of Alzheimer's disease. Other environmental and genetic factors come into play in the development of Alzheimer's.

SNP 1 - rs429358	SNP 2 - rs7412	Name
T	T	ε2
T	C	ε3
C	C	ε4

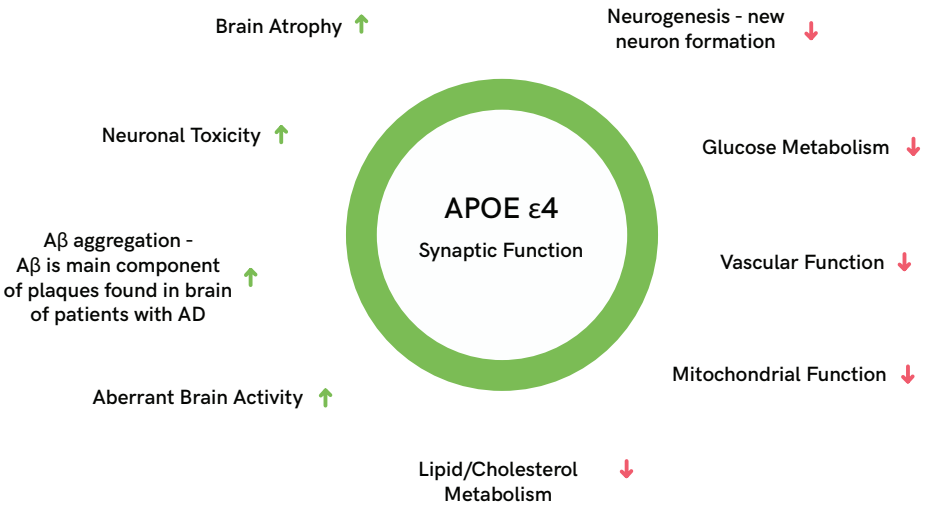
The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

Association of APOE genetic variations and aging rate



Consistent with previous longevity studies, individuals (>66 years old) with APOE ε3/ε2 genetic variation exhibit slower aging rates. While individuals carrying the APOE ε4/ε4 variation demonstrate faster aging rate.

APOE ε4 association with various disease pathogenesis



The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

MTHFR

What is MTHFR?

MTHFR gene stands for methylenetetrahydrofolate reductase. Each person carries two copies of the MTHFR gene, inherited from each parent. The MTHFR gene encodes an enzyme involved in the following:

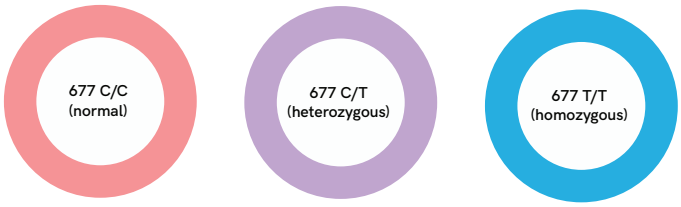
- Metabolizing folate (also called folic acid or vitamin B9).
- Conducting the process of methylation in cells.

The MTHFR gene has been heavily researched in association with human diseases such as cardiovascular disease, pregnancy complications, and various cancers.

What are the MTHFR "variants"?

Within the MTHFR gene, there are two well studied SNPs - rs1801131 and rs1801133, wherein variation results in reduced enzymatic activity and subsequently impacts overall well being. These variants are common. In the United States, about 25% of Hispanics, and 10-15% of Caucasians have two copies of C677T.

If you have an MTHFR mutation, your MTHFR gene function may be reduced. This may lead to elevated homocysteine levels in the blood, resulting in various health complications including homocystinuria, an increased risk of heart disease, stroke, high blood pressure and blood clots.



Genotype	SNP 1 - CC	SNP 1 - CT	SNP 1 - TT
SNP 2 - AA	100% enzyme activity	66% enzyme activity	25% enzyme activity
SNP 2 - AC	83% enzyme activity	48% enzyme activity	Not analyzed
SNP 2 - CC	61% enzyme activity	Not analyzed	Not analyzed

Do the MTHFR genetic variants have an impact on DNAge prediction?

The MTHFR gene encodes methylenetetrahydrofolate reductase, an enzyme that conducts the process of methylation in cells. However, there are no significant differences in global DNA methylation in individuals with MTHFR genetic variants.

Additionally, based on our current population database, MTHFR genetic variants do not exhbit statistically significant impact on DNAge prediction and aging rate.

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

References

1. Bocklandt S, Lin W, Sehl ME, Sánchez FJ, Sinsheimer JS, Horvath S, Vilain E. Epigenetic predictor of age. PLoS One. 2011;6(6):e14821.

2. Horvath, S. et al. Accelerated epigenetic aging in Down syndrome. Aging Cell 14, 491–495 (2015).

3. Horvath, S. et al. An epigenetic clock analysis of race/ethnicity, sex, and coronary heart disease. Genome Biol 17, 171 (2016).

4. Horvath et al. - 2016 - An epigenetic clock analysis of raceethnicity, se.pdf.

5. Hannum, G. et al. Genome-wide Methylation Profiles Reveal Quantitative Views of Human Aging Rates. Molecular Cell 49, 359–367 (2013).

6. Horvath, S. et al. Huntington's disease accelerates epigenetic aging of human brain and disrupts DNA methylation levels. Aging 8, 1485–1512 (2016).

7. Davis, E. G. et al. Accelerated DNA methylation age in adolescent girls: associations with elevated diurnal cortisol and reduced hippocampal volume. Transl Psychiatry 7, e1223–e1223 (2017).

8. Dozmorov, M. G., Coit, P., Maksimowicz-McKinnon, K. & Sawalha, A. H. Age-associated DNA methylation changes in naive CD4 + T cells suggest an evolving autoimmune epigenotype in aging T cells. Epigenomics 9, 429–445 (2017).

9. Solovev, I., Shaposhnikov, M. & Moskalev, A. Multi-omics approaches to human biological age estimation. Mechanisms of Ageing and Development 185, 111192 (2020).

10. Salameh, Y., Bejaoui, Y. & El Hajj, N. DNA Methylation Biomarkers in Aging and Age-Related Diseases. Front. Genet. 11, 171 (2020).

11. Horvath, S. et al. Obesity accelerates epigenetic aging of human liver. Proceedings of the National Academy of Sciences 111, 15538–15543 (2014).

12. Horvath, S. et al. Decreased epigenetic age of PBMCs from Italian semi-supercentenarians and their offspring. Aging 7, 1159–1170 (2015).

13. Hayano, M. et al. DNA Break-Induced Epigenetic Drift as a Cause of Mammalian Aging. http://biorxiv.org/lookup/doi/10.1101/808659 (2019) doi:10.1101/808659.

14. Dick, K. J. et al. DNA methylation and body-mass index: a genome-wide analysis. The Lancet 383, 1990–1998 (2014).

15. Geurts, Y. M. et al. Novel associations between blood DNA methylation and body mass index in middle-aged and older adults. Int J Obes 42, 887–896 (2018).

16. Wahl, S. et al. Epigenome-wide association study of body mass index, and the adverse outcomes of adiposity. Nature 541, 81–86 (2017).

17. Sun, D. et al. Body Mass Index Drives Changes in DNA Methylation: A Longitudinal Study. Circ Res 125, 824–833 (2019).

18. Tam, B. T., Morais, J. A. & Santosa, S. Obesity and ageing: Two sides of the same coin. Obesity Reviews 21, (2020).

19. Walaszczyk, E. et al. DNA methylation markers associated with type 2 diabetes, fasting glucose and HbA1c levels: a systematic review and replication in a case–control sample of the Lifelines study. Diabetologia 61, 354–368 (2018).

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

20. Ronn, T. et al. Impact of age, BMI and HbA1c levels on the genome-wide DNA methylation and mRNA expression patterns in human adipose tissue and identification of epigenetic biomarkers in blood. Human Molecular Genetics ddv124 (2015) doi:10.1093/hmg/ddv124.

21. Willmer, T., Johnson, R., Louw, J. & Pheiffer, C. Blood-Based DNA Methylation Biomarkers for Type 2 Diabetes: Potential for Clinical Applications. Front. Endocrinol. 9, 744 (2018).

22. Ling, C. & Rönn, T. Epigenetics in Human Obesity and Type 2 Diabetes. Cell Metabolism 29, 1028–1044 (2019).

23. Cardona, A. et al. Epigenome-Wide Association Study of Incident Type 2 Diabetes in a British Population: EPIC-Norfolk Study. Diabetes 68, 2315–2326 (2019).

24. Juvinao-Quintero, D. L. et al. DNA methylation of blood cells is associated with prevalent type 2 diabetes in a meta-analysis of four European cohorts. Clin Epigenet 13, 40 (2021).

25. Ma, J. et al. A Peripheral Blood DNA Methylation Signature of Hepatic Fat Reveals a Potential Causal Pathway for Nonalcoholic Fatty Liver Disease. Diabetes 68, 1073–1083 (2019).

26. Chambers, J. C. et al. Epigenome-wide association of DNA methylation markers in peripheral blood from Indian Asians and Europeans with incident type 2 diabetes: a nested case-control study. The Lancet Diabetes & Endocrinology 3, 526–534 (2015).

27. Ahmed, S. A. H., Ansari, S. A., Mensah-Brown, E. P. K. & Emerald, B. S. The role of DNA methylation in the pathogenesis of type 2 diabetes mellitus. Clinical Epigenetics 12, 104 (2020).

28. Jhun, M.-A. et al. A multi-ethnic epigenome-wide association study of leukocyte DNA methylation and blood lipids. Nat Commun 12, 3987 (2021).

29. Muka, T. et al. The role of global and regional DNA methylation and histone modifications in glycemic traits and type 2 diabetes: A systematic review. Nutrition, Metabolism and Cardiovascular Diseases 26, 553–566 (2016).

30. Wilson, L. E., Harlid, S., Xu, Z., Sandler, D. P. & Taylor, J. A. An epigenome-wide study of body mass index and DNA methylation in blood using participants from the Sister Study cohort. Int J Obes 41, 194–199 (2017).

31. Mendelson, M. M. et al. Association of Body Mass Index with DNA Methylation and Gene Expression in Blood Cells and Relations to Cardiometabolic Disease: A Mendelian Randomization Approach. PLoS Med 14, e1002215 (2017).

32. Aslibekyan, S. et al. Epigenome-wide study identifies novel methylation loci associated with body mass index and waist circumference: Epigenetics of Obesity. Obesity 23, 1493–1501 (2015).

33. Rohde, K. et al. Genetics and epigenetics in obesity. Metabolism 92, 37–50 (2019).

34. Campanella, G. et al. Epigenome-wide association study of adiposity and future risk of obesity-related diseases. Int J Obes 42, 2022–2035 (2018).

35. Lupo, P. J. et al. DNA methylation and obesity in survivors of pediatric acute lymphoblastic leukemia (ALL): A report from the Childhood Cancer Survivor Study (CCSS). 1.

36. Kriebel, J. et al. Association between DNA Methylation in Whole Blood and Measures of Glucose Metabolism: KORA F4 Study. PLoS ONE 11, e0152314 (2016).

37. Arpón, A. et al. Epigenome-wide association study in peripheral white blood cells involving insulin resistance. Sci Rep 9, 2445 (2019).

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

38. Mittelstraß, K. & Waldenberger, M. DNA methylation in human lipid metabolism and related diseases: Current Opinion in Lipidology 29, 116–124 (2018).

39. Pfeiffer, L. et al. DNA Methylation of Lipid-Related Genes Affects Blood Lipid Levels. Circulation. Cardiovascular genetics 8, 334–342 (2015).

40. Hedman, Å. K. et al. Epigenetic Patterns in Blood Associated With Lipid Traits Predict Incident Coronary Heart Disease Events and Are Enriched for Results From Genome-Wide Association Studies. Circ Cardiovasc Genet 10, (2017).

41. Gomez-Alonso, M. del C. et al. DNA methylation and lipid metabolism: an EWAS of 226 metabolic measures. Clin Epigenet 13, 7 (2021).

42. Irvin, M. R. et al. Epigenome-Wide Association Study of Fasting Blood Lipids in the Genetics of Lipid Lowering Drugs and Diet Network Study. Circulation 130, 565–572 (2014).

43. Tobi, E. W. et al. DNA methylation as a mediator of the association between prenatal adversity and risk factors for metabolic disease in adulthood. Sci. Adv. 4, eaao4364 (2018).

44. Akinyemiju, T. et al. Epigenome-wide association study of metabolic syndrome in African-American adults. Clin Epigenet 10, 49 (2018).

45. Kho, M. et al. Epigenetic loci for blood pressure are associated with hypertensive target organ damage in older African Americans from the genetic epidemiology network of Arteriopathy (GENOA) study. BMC Med Genomics 13, 131 (2020).

46. Biomarkers of Human Aging. vol. 10 (Springer International Publishing, 2019).

47. Irvin, M. R. et al. Metabolic and inflammatory biomarkers are associated with epigenetic aging acceleration estimates in the GOLDN study. Clin Epigenet 10, 56 (2018).

48. Sayols-Baixeras, S. et al. Identification and validation of seven new loci showing differential DNA methylation related to serum lipid profile: an epigenome-wide approach. The REGICOR study. Human Molecular Genetics 25, 4556–4565 (2016).

49. Jones, A. C., Irvin, M. R., Claas, S. A. & Arnett, D. K. Lipid Phenotypes and DNA Methylation: a Review of the Literature. Curr Atheroscler Rep 23, 71 (2021).

50. Dayeh, T. et al. DNA methylation of loci within ABCG1 and PHOSPHO1 in blood DNA is associated with future type 2 diabetes risk. Epigenetics 11, 482–488 (2016).

51. Krause, C. et al. Critical evaluation of the DNA-methylation markers ABCG1 and SREBF1 for Type 2 diabetes stratification. Epigenomics 11, 885–897 (2019).

52. Qie, R. et al. Association of ABCG1 gene methylation and its dynamic change status with incident type 2 diabetes mellitus: the Rural Chinese Cohort Study. J Hum Genet 66, 347–357 (2021).

53. Richard, M. A. et al. DNA Methylation Analysis Identifies Loci for Blood Pressure Regulation. The American Journal of Human Genetics 101, 888–902 (2017).

54. Irvin, M. R., Jones, A. C., Claas, S. A. & Arnett, D. K. DNA Methylation and Blood Pressure Phenotypes: A Review of the Literature. American Journal of Hypertension 34, 267–273 (2021).

55. Das, M. et al. Association of DNA Methylation at CPT1A Locus with Metabolic Syndrome in the Genetics of Lipid Lowering Drugs and Diet Network (GOLDN) Study. PLoS ONE 11, e0145789 (2016).

56. Rathore, R., Schutt, C. R. & Van Tine, B. A. PHGDH as a mechanism for resistance in metabolically-driven cancers. CDR (2020) doi:10.20517/cdr.2020.46.

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

57. Mizuno, G. et al. Association between the extent of DNA methylation at the CpG sites of HIF3A and parameters of obesity in the general Japanese population. http://biorxiv.org/lookup/doi/10.1101/2020.11.30.403709 (2020) doi:10.1101/2020.11.30.403709.

58. Huang, T. et al. DNA Methylation Variants at HIF3A Locus, B-Vitamin Intake, and Long-term Weight Change: Gene-Diet Interactions in Two U.S. Cohorts. Diabetes 64, 3146–3154 (2015).

59. Main, A. M. et al. DNA methylation and gene expression of HIF3A: cross-tissue validation and associations with BMI and insulin resistance. Clinical Epigenetics 8, 89 (2016).

60. Shen, J. et al. HIF3A DNA methylation, obesity and weight gain, and breast cancer risk among Mexican American women. Obesity Research & Clinical Practice 14, 548–553 (2020).

61. Wang, Y. et al. High Glucose Induces Lipid Accumulation via 25-Hydroxycholesterol DNA-CpG Methylation. iScience 23, 101102 (2020).

62. Ali, O. et al. Methylation of SOCS3 is inversely associated with metabolic syndrome in an epigenome-wide association study of obesity. Epigenetics 11, 699–707 (2016).

63. Wang, L. et al. Combined effects of progesterone and SOCS3 DNA methylation on T2DM: a case–control study. Clin Epigenet 13, 181 (2021).

64. K., Zhang, X., Wang, Z., Hu, Y. & Sinha, R. Epigenome-wide association analysis revealed that SOCS3 methylation influences the effect of cumulative stress on obesity. Biological Psychology 131, 63–71 (2018).

65. Gao, Xu et al. Comparative validation of an epigenetic mortality risk score with three aging biomarkers for predicting mortality risks among older adult males. International Journal of Epidemiology. 48, 6, 1958-1971. (2019).

66. Zaghlool, S. B. et al. Deep molecular phenotypes link complex disorders and physiological insult to CpG methylation. Human Molecular Genetics 27, 1106–1121 (2018).

67. Kankaanpää, A. et al. Leisure-Time and Occupational Physical Activity Associates Differently with Epigenetic Aging. Medicine & Science in Sports & Exercise 53, 487–495 (2021).

68. Zannas, A. S. et al. Lifetime stress accelerates epigenetic aging in an urban, African American cohort: relevance of glucocorticoid signaling. Genome Biol 16, 266 (2015).

69. Hughes, A. et al. Socioeconomic Position and DNA Methylation Age Acceleration Across the Life Course. American Journal of Epidemiology 187, 2346–2354 (2018).

70. White, A. J., Kresovich, J. K., Xu, Z., Sandler, D. P. & Taylor, J. A. Shift work, DNA methylation and epigenetic age. International Journal of Epidemiology 48, 1536–1544 (2019).

71. Ozbay, F. et al. social support and resilience to stress: from neurobiology to clinical practice. Psychiatry (Edgmont) 4, 35–40 (2007).

72. Ma, X. et al. The Effect of Diaphragmatic Breathing on Attention, Negative Affect and Stress in Healthy Adults. Front. Psychol. 8, 874 (2017).

73. Li, J. et al. Exposure to Polycyclic Aromatic Hydrocarbons and Accelerated DNA Methylation Aging. Environ Health Perspect 126, 067005 (2018).

74. van der Laan, L. et al. Epigenetic aging biomarkers and occupational exposure to benzene, trichloroethylene and formaldehyde. Environment International 158, 106871 (2022).

75. Rider, C. F. & Carlsten, C. Air pollution and DNA methylation: effects of exposure in humans. Clinical Epigenetics 11, 131 (2019).

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

76. Rebelo-Marques, A. et al. Aging Hallmarks: The Benefits of Physical Exercise. Front. Endocrinol. 9, 258 (2018).

77. Spólnicka, M. et al. Modified aging of elite athletes revealed by analysis of epigenetic age markers. Aging 10, 241–252 (2018).

78. Rosen, A. D. et al. DNA methylation age is accelerated in alcohol dependence. Transl Psychiatry 8, 182 (2018).

79. Karabegović, I. et al. Epigenome-wide association meta-analysis of DNA methylation with coffee and tea consumption. Nat Commun 12, 2830 (2021).

80. Gallardo-Escribano, C. et al. Epigenetic approach in obesity: DNA methylation in a prepubertal population which underwent a lifestyle modification. Clin Epigenet 12, 144 (2020).

81. Jacka, F. N. et al. A randomised controlled trial of dietary improvement for adults with major depression (the 'SMILES' trial). BMC Med 15, 23 (2017).

82. American Diabetes Association. 5. Facilitating Behavior Change and Well-being to Improve Health Outcomes: Standards of Medical Care in Diabetes—2020. Diabetes Care 43, S48–S65 (2020).

83. Quach, A. et al. Epigenetic clock analysis of diet, exercise, education, and lifestyle factors. Aging 9, 419–446 (2017).

84. Lillycrop, K. A., Hoile, S. P., Grenfell, L. & Burdge, G. C. DNA methylation, ageing and the influence of early life nutrition. Proc. Nutr. Soc. 73, 413–421 (2014).

85. Nakagawa, S., Lagisz, M., Hector, K. L. & Spencer, H. G. Comparative and meta-analytic insights into life extension via dietary restriction: Dietary restriction and longevity: meta-analysis. Aging Cell 11, 401–409 (2012).

86. Colman, R. J. et al. Caloric restriction delays disease onset and mortality in rhesus monkeys. Science (New York, N.Y.) 325, 201–204 (2009).

87. Hahn, O. et al. Dietary restriction protects from age-associated DNA methylation and induces epigenetic reprogramming of lipid metabolism. Genome Biol 18, 56 (2017).

88. Simons, M. J. P., Koch, W. & Verhulst, S. Dietary restriction of rodents decreases aging rate without affecting initial mortality rate – a meta-analysis. Aging Cell 12, 410–414 (2013).

89. Yaskolka Meir, A. et al. Lifestyle weight-loss intervention may attenuate methylation aging: the CENTRAL MRI randomized controlled trial. Clin Epigenet 13, 48 (2021).

90. Petersen, C. L., Christensen, B. C. & Batsis, J. A. Weight management intervention identifies association of decreased DNA methylation age with improved functional age measures in older adults with obesity. Clin Epigenet 13, 46 (2021).

91. Ma, J. et al. Whole Blood DNA Methylation Signatures of Diet Are Associated With Cardiovascular Disease Risk Factors and All-Cause Mortality. Circ: Genomic and Precision Medicine 13, (2020).

92. Sofi, F., Abbate, R., Gensini, G. F. & Casini, A. Accruing evidence on benefits of adherence to the Mediterranean diet on health: an updated systematic review and meta-analysis. The American Journal of Clinical Nutrition 92, 1189–1196 (2010).

93. Belsky, Daniel W et al. "Change in the Rate of Biological Aging in Response to Caloric Restriction: CALERIE Biobank Analysis." The journals of gerontology. Series A, Biological sciences and medical sciences vol. 73,1 (2017): 4-10. doi:10.1093/gerona/glx096

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.

94. Liu, C.-C., Liu, C.-C., Kanekiyo, T., Xu, H. & Bu, G. Apolipoprotein E and Alzheimer disease: risk, mechanisms and therapy. Nature Reviews. Neurology 9, 106–118 (2013).

95. Walker, R. M. et al. Identification of epigenome-wide DNA methylation differences between carriers of APOE ε4 and APOE ε2 alleles. Genome Med 13, 1 (2021).

96. Van der Put, N. M. et al. A second common mutation in the methylenetetrahydrofolate reductase gene: an additional risk factor for neural-tube defects? American Journal of Human Genetics 62, 1044–1051 (1998).

97. Dean, L. Methylenetetrahydrofolate Reductase Deficiency. in Medical Genetics Summaries (eds. Pratt, V. M. et al.) (National Center for Biotechnology Information (US), 2012).

98. CDC. MTHFR Gene and Folic Acid. Centers for Disease Control and Prevention (2020).

The Epimorphy myDNAge® service is an epigenetic age test determination for informational and educational purposes only for those 21 years and older. The information provided to you from the test is not health information or medical data nor is it intended to be used to screen, diagnose, treat, prevent, or assess risk of any disease or condition. This Service has not been cleared or approved by U. S. Food and Drug Administration. Consult a physician or other healthcare provider if you have questions or concerns about the information provided to you.