TRUAGE BY TRUDIAGNOSTIC

OMICm Age

This report calculates biological age by examining age-associated methylation patterns at approximately one million locations on your DNA, using the novel OMICm Age algorithm.

Developed By TruDiagnostic's Bioinformatics & Research Department

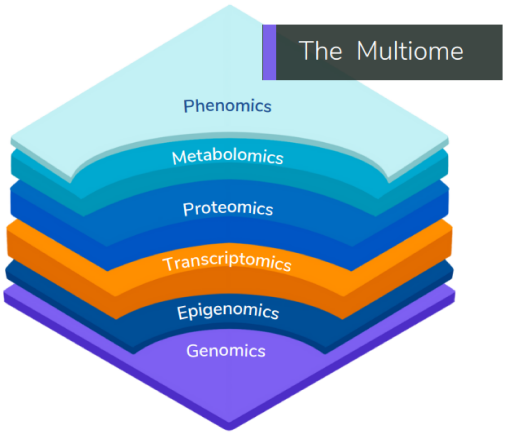
A NEW AGING ALGORITHM

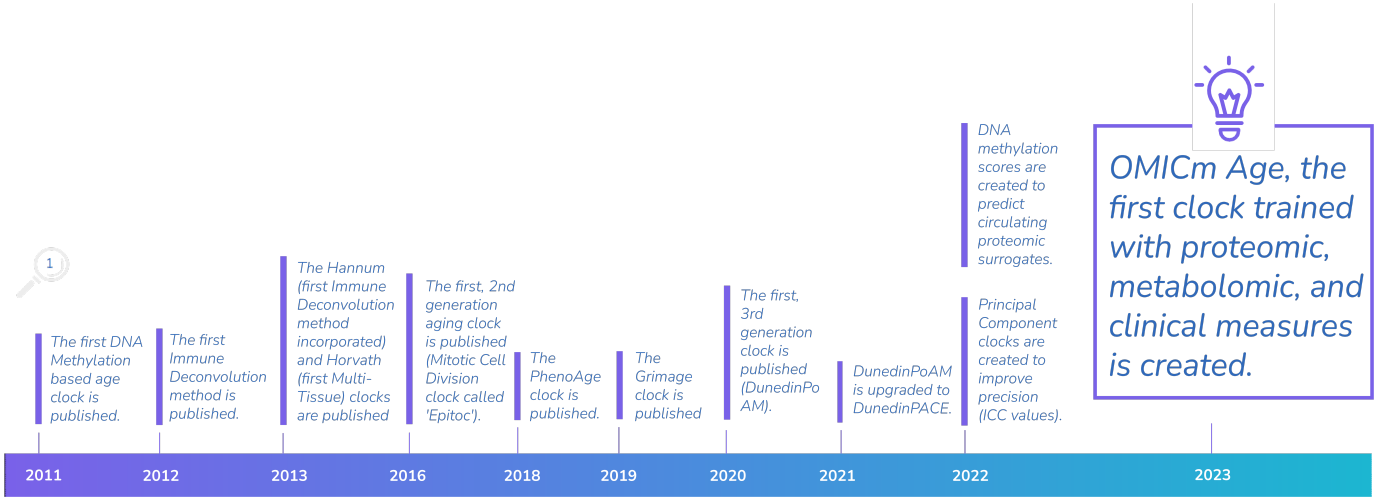
Raising the bar on measuring aging.

When TruDiagnostic was founded in 2020, we set out on a mission to create the best scientific algorithm (clock) that analyzes epigenetic patterns to accurately quantify biological age. To do this, we needed an extensive amount of data, which is why we partnered with researchers from Harvard University and Partners Biobank.

This biobank included thousands of samples saved from over the last 50 years. With these samples, **we were able to collect the extensive amount of interconnected biodata needed to create the most accurate predictors of biological aging.**

This process has taken us almost three years to finalize, but we are proud to announce the completion of the best biological age clock ever created; the **OMICm Age** algorithm.





OUR APPROACH

Multi Omics & Biological Aging.

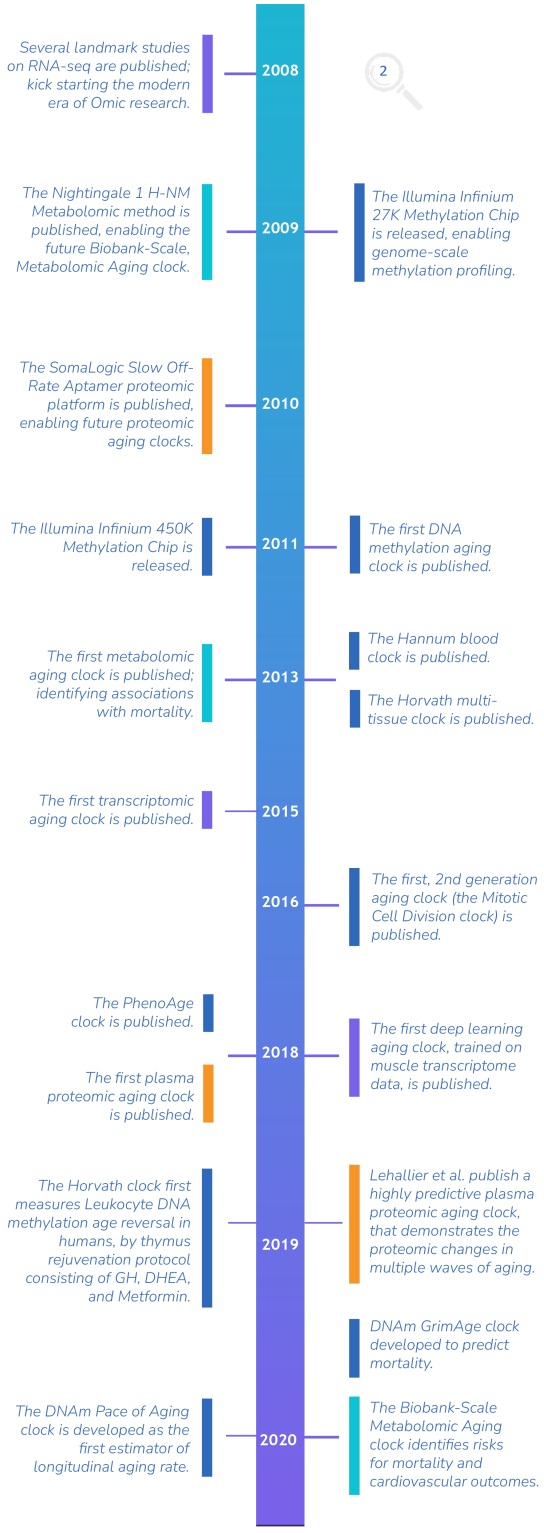
When the Human Genome Project (an initiative to map the entire human genome) was first announced decades ago, many people thought the results would inform us about everything related to human biology. While it was a great project, the actionable health information gained from its efforts left many people disappointed. One reason why is that genetic composition is only one small piece of the puzzle.

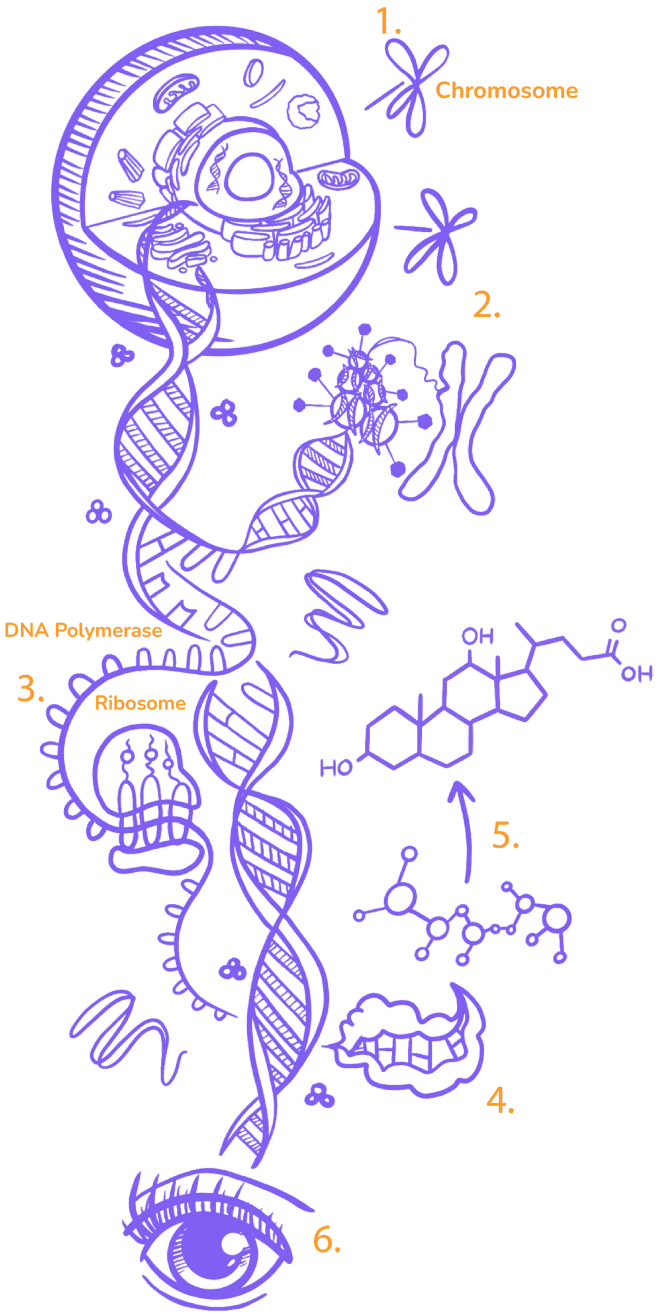
We now know that **the functionality of your body, as well as your health outcomes (phenotypes), are a result of much more than just your DNA.** Your epigenetics and transcriptome, the peptides and proteins in your body (proteome), and the metabolites from your body's processes and environmental exposures are all crucial factors in how your biology operates. This large picture of interconnected cellular processes is often called the multiome (Multi Omics) and it is a combination of all the different measurements we can perform on the body.

Thus, to create the best biological age clock, we didn't want to just measure epigenetics. We wanted to measure the entire multiome. So, we did! **In 5,000 people, we used advanced analysis techniques to quantify all biomarkers that make up the multiome.' Proteins, metabolites, and DNA methylation altogether were measured in only 1500 subjects. We used these individuals to train the epigenetic biomarker proxies (EBPs) for proteins and metabolites and, later on, we quantified these EBP in the 5000 subjects with DNA methylation.** We used Whole Exome Sequencing. Untargeted Plasma Proteomics, Plasma Metabolomics, as well as Clinical Data and Outcome Data for our large group (cohort). Together, this novel data allows for an unmatched resolution in quantifying the whole body's aging process. It also allows us to view aging throughout the multiome, through the lens of DNA methylation.

In our initial publication regarding the research and findings used to develop our OMICm Age algorithm, we **showed that this clock is better at predicting health and aging outcomes** than any other methylation age clock to date.

Epigenomics
Transcriptomics
Proteomics
Metabolomics





1. Genomics

The study of the genes housed in our DNA. Our DNA, located in the nucleus of our cells, contains sections of instructions (genes) that tell a cell how to behave. Your genetics stay the same from conception to death.

2. Epigenomics

The study of how our genes are modified. Epigenetic molecules interact with our DNA, either amplifying or silencing certain instructions. These interactions change throughout your lifetime.

3. Transcriptomics

The study of how our genes turn into actionable RNA. During transcription, molecules called RNA copy the instructions of our DNA; skipping over or boosting sections based on the epigenetic patterns at that location.

4. Proteomics

The study of how proteins function. Proteins are created by RNA, and perform most of the work within a cell. Antibodies, enzymes, and hormones are all types of protein functions.

5. Metabolomics

The study of the chemical processes produced by protein interactions. Metabolites are a by-product of proteins hard at work, and are used to help break down food, drugs, chemicals, or the body's own tissue.

6. Phenomics

The study of observable traits such as eye, skin, and hair color. Epigenetics can curate those instructions, and the resulting proteins and metabolites impact your biology to result in a physical expression.

PROVIDED BY: TruDiagnostic™

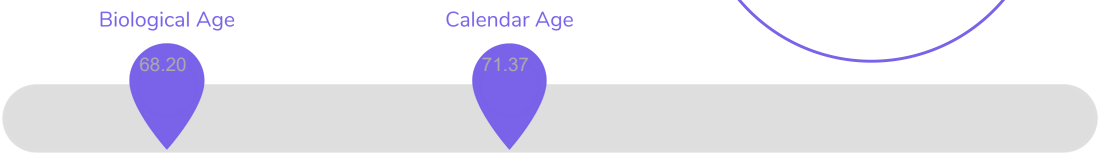
Your Results.

DISCLAIMER: All population graphs included in this report are based off of data from thousands of research participants and TruAge test takers. Unless otherwise specified, population graphs are included to provide context to your results, but are not necessarily reflections of individual scores.

68.20

YEARS OLD

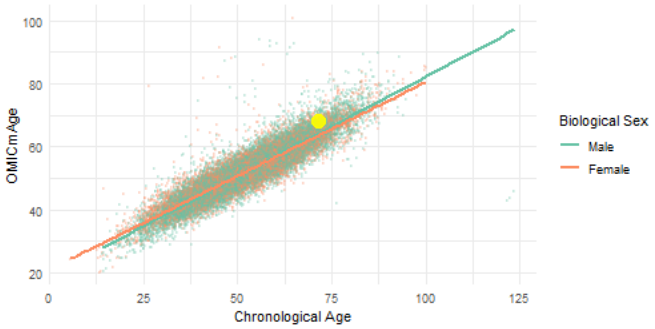
OMICm Age



Your OMICm Age is

LOWER THAN

your calendar age by **3.17** years.



YOUR OMICm Age IS IN THE:

89.31th

PERCENTILE MEANING THAT YOUR OMICm AGE IS HIGHER THAN **89.31%** OF THE POPULATION AT YOUR SAME CHRONOLOGICAL AGE .

YOUR RISK OF DISEASE

DISCLAIMER: The following, personalized risk scores were calculated based off of observed and validated patterns in data, from thousands of research participants involved in our Harvard University and TruDiagnostic partnered study. This cohort is believed to be a strong sample representation of larger population data.

Aging has been scientifically proven to be the number one risk factor for major chronic diseases world-wide. Accelerated aging (having an older biological age than your calendar age) increases your risk of disease with each year, and having a younger biological age decreases these risks.

Your OMICm Biological Age can represent an increase or decrease risk of Death, Cancer, Heart Disease, Stroke, Type 2 Diabetes, COPD, and Depression.

-28%
Disease Risk

Reflects your current risk. A -28% score means that your risk is 28% lower compared to people of your same chronological age.

47%
Disease Risk

Reflects your current risk. A 47% score means that your risk is 47% higher compared to people of your same chronological age.

31%

Reflects your potential risk score based on potential changes to your biological age.

DEATH

-3 YEARS	-1 YEAR		+1 YEAR	+3 YEARS
-0.87%	30%	48.87% Disease Risk	70.49%	123.61%

CANCER

-3 YEARS	-1 YEAR		+1 YEAR	+3 YEARS
-0.39%	12.52%	19.59% Disease Risk	27.11%	43.59%

STROKE

-3 YEARS	-1 YEAR		+1 YEAR	+3 YEARS
-0.43%	13.96%	21.93% Disease Risk	30.45%	49.32%

HEART DISEASE

-3 YEARS	-1 YEAR		+1 YEAR	+3 YEARS
-0.47%	15.22%	23.98% Disease Risk	33.4%	54.45%

TYPE 2 DIABETES

-3 YEARS	-1 YEAR		+1 YEAR	+3 YEARS
-0.4%	12.72%	19.93% Disease Risk	27.59%	44.41%

COPD

-3 YEARS	-1 YEAR		+1 YEAR	+3 YEARS
-0.26%	8.19%	12.68% Disease Risk	17.36%	27.31%

DEPRESSION

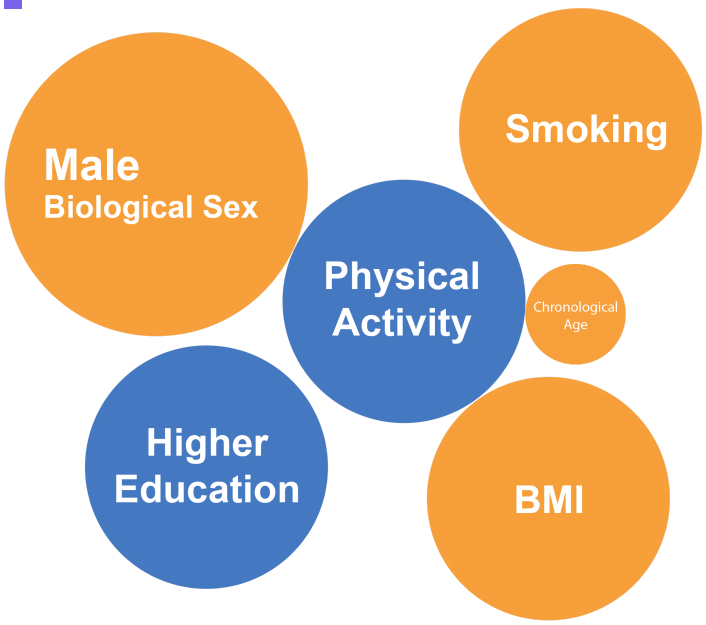
-3 YEARS	-1 YEAR		+1 YEAR	+3 YEARS
-0.25%	7.91%	12.25% Disease Risk	16.76%	26.33%

- END OF DISEASE RISK RESULTS -

In the chart below, you can see some of the top factors that contribute to an increase (yellow) or decrease (blue) of OMICm Age.

While some influences like sex and chronological age are innate and unchangeable, **mostt contributing factors like smoking and physical activity can be modified.** It is important to note that an influence, or association, is not necessarily a cause. The chart below shows **research-backed associations with a higher or lower biological age.** These factors may or may not be direct causes, however, strong age-related trends have been distinguished.

HARVARD BIOLOGICAL AGING COHORT



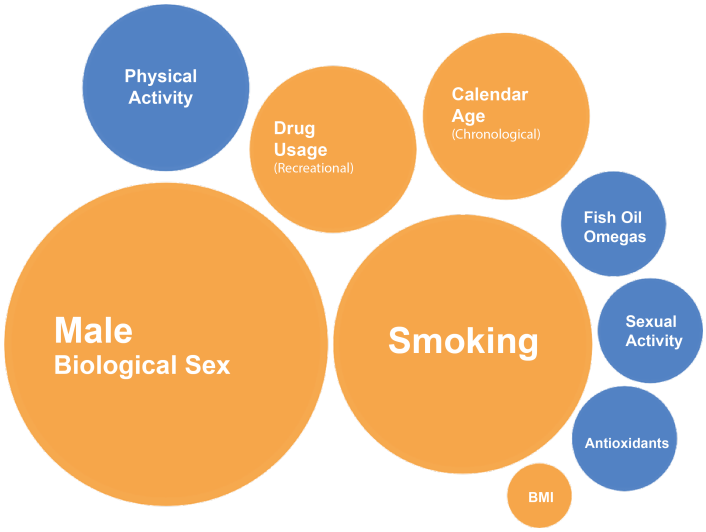
Associated with
lower
OMICm Age

Associated with
higher
OMICm Age

TRU COHORT

Associated with
lower
OMICm Age

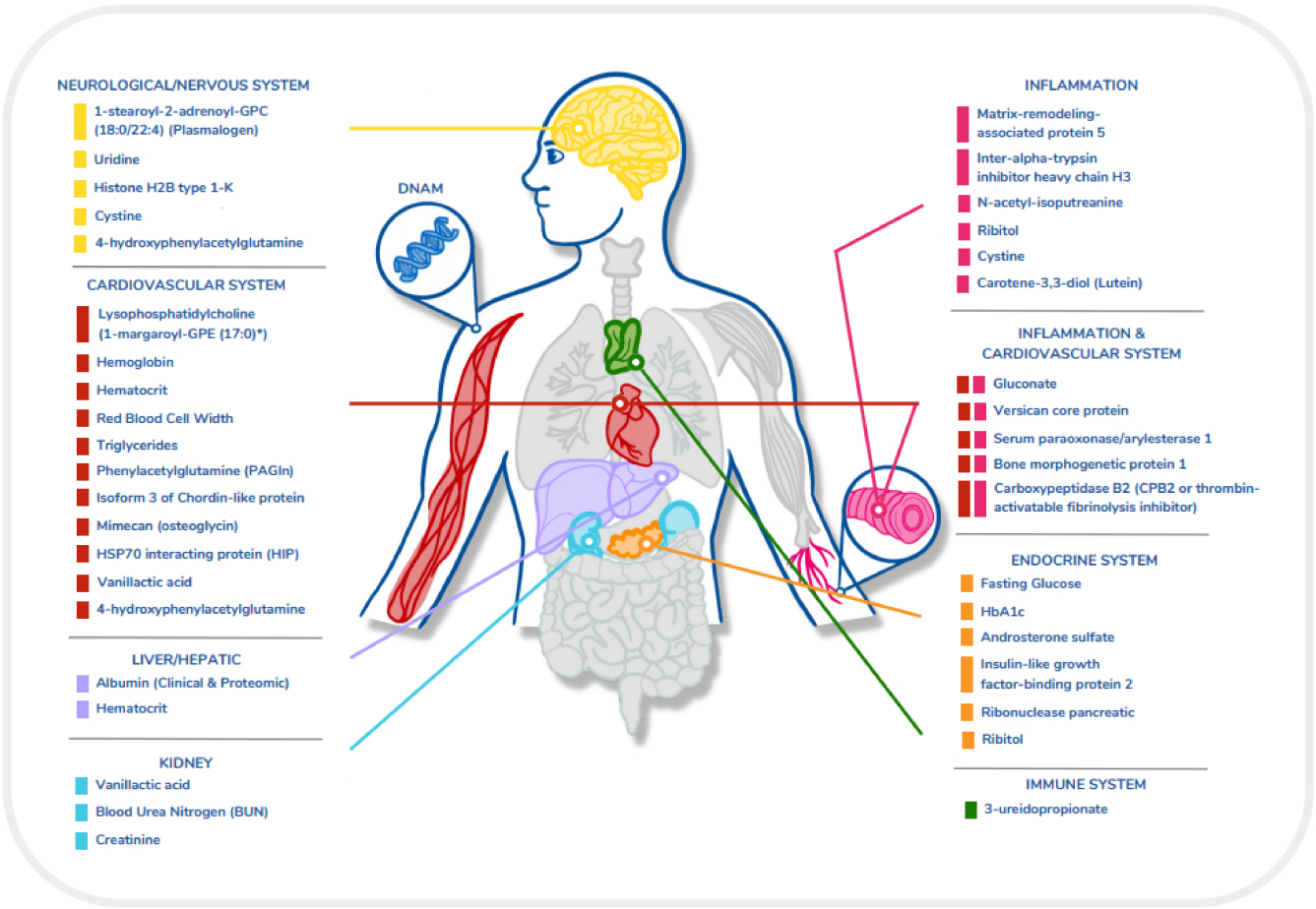
Associated with
higher
OMICm Age



THE EPIGENETIC BIOMARKER PROXIES DRIVING YOUR BIOLOGICAL AGE

We use epigenetic biomarker proxies (EBPs) scores to predict genomics, transcriptomics, proteomics, and metabolomics sum values that are positive for your aging, and some that are negative for your aging. In the graph below you will see the factors contributing to your aging the most. If a bar is above zero, it's increasing your OMICm Age, if below zero, it is decreasing your OMICm Age.

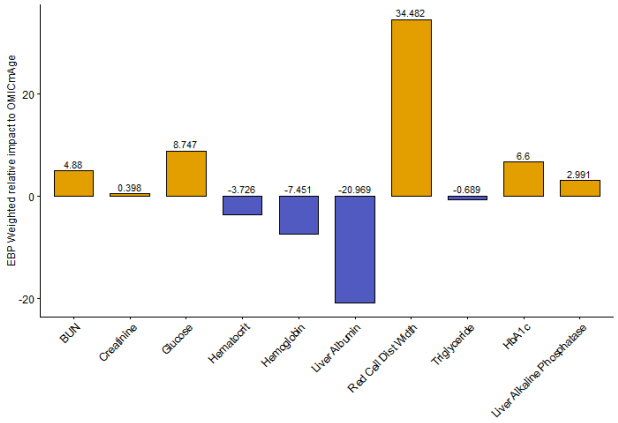
BODY SYSTEMS CONTRIBUTING TO THE DEVELOPMENT OF OMICAGE THROUGH OMICS



Neurological/Nervous System | Cardiovascular system | DNAm | Liver/Hepatic
Immune System | Kidney | Endocrine System | Inflammation

CLINICAL FACTORS

Your Clinical Epigenetic Biomarker Proxies (EBP)

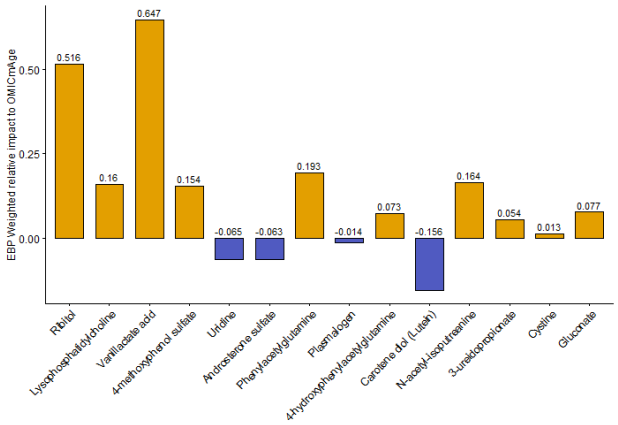


Associated ***higher*** OMICm Age

Associated ***lower*** OMICm Age

METABOLITES

Your Metabolites Epigenetic Biomarker Proxies (EBP)

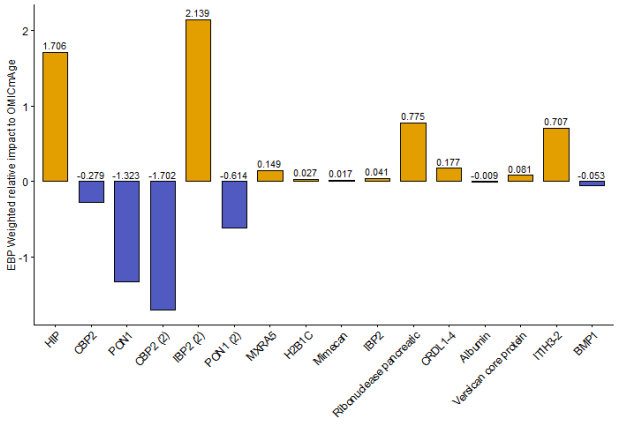


Associated ***higher*** OMICm Age

Associated ***lower*** OMICm Age

PROTEINS

Your Protein Epigenetic Biomarker Proxies (EBP)



Associated ***higher*** OMICm Age

Associated ***lower*** OMICm Age

CLINICAL RESULTS

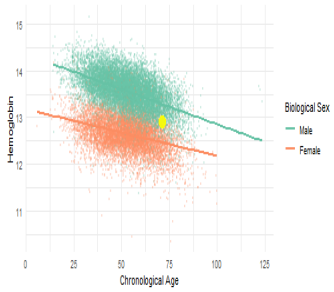
EXPANDED

Hemoglobin

HIGHER RATES ASSOCIATED WITH IMPROVED OMIC AGE

12.89 g/dl

Your **Hemoglobin** is higher than **44.3%** of the population at your same calendar age and sex.

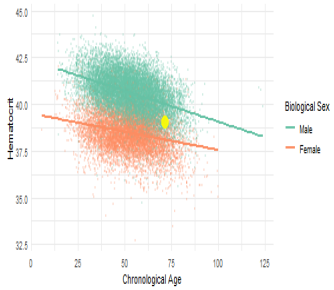


Hematocrit

HIGHER RATES ASSOCIATED WITH IMPROVED OMIC AGE

39.04 L/L

Your **Hematocrit** is higher than **43.09%** of the population at your same calendar age and sex.



Alkaline Phosphatase (ALP)

LOWER RATES ASSOCIATED WITH IMPROVED OMIC AGE

85.75 U/L

Your **Alkaline Phosphatase (ALP)** is higher than **49.52%** of the population at your same calendar age and sex.

HbA1c

LOWER RATES ASSOCIATED WITH IMPROVED OMIC AGE

6.36 %

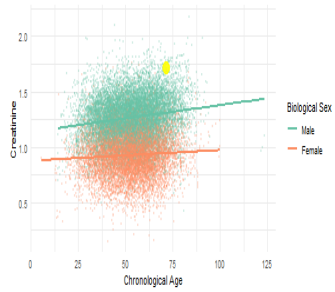
Your **HbA1c** is higher than **58.29%** of the population at your same calendar age and sex.

Creatinine

LOWER RATES ASSOCIATED WITH IMPROVED OMIC AGE

1.71 mg/dL

Your **Creatinine** is higher than **98.52%** of the population at your same calendar age and sex.

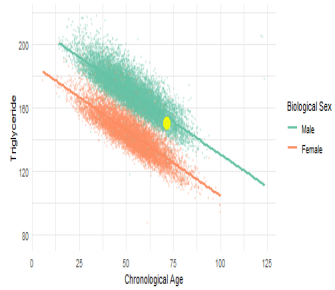


Triglycerides

HIGHER RATES ASSOCIATED WITH IMPROVED OMIC AGE

150.39 mmol/L

Your **Triglycerides** is higher than **57.6%** of the population at your same calendar age and sex.

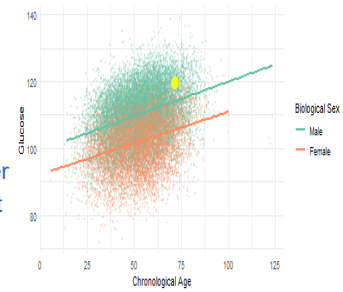


Fasting Glucose

LOWER RATES ASSOCIATED WITH IMPROVED OMIC AGE

119.74 mmol/L or in mg/dL

Your **Fasting Glucose** is higher than **84.1%** of the population at your same calendar age and sex.

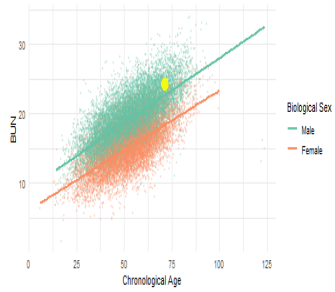


Blood Urea Nitrogen (BUN)

LOWER RATES ASSOCIATED WITH IMPROVED OMIC AGE

24.2 mg/dLor in mmol/L

Your **Blood Urea Nitrogen (BUN)** is higher than **82.71%** of the population at your same calendar age and sex.

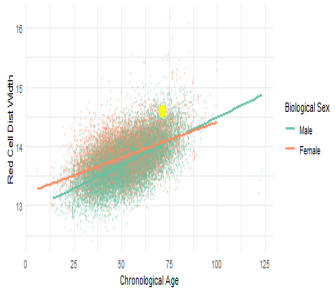


Red Blood Cell Width

LOWER RATES ASSOCIATED WITH
IMPROVED OMIC AGE

14.6 fL

Your **Red Blood Cell Width** is higher than **96.43%** of the population at your same calendar age and sex.

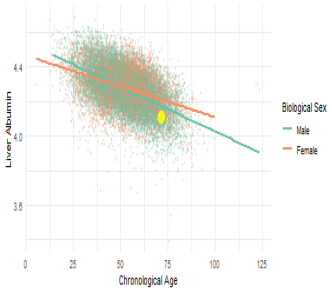


Albumin (Clinical)

HIGHER RATES ASSOCIATED WITH
IMPROVED OMIC AGE

4.1 g/dL

Your **Albumin (Clinical)** is higher than **25.19%** of the population at your same calendar age and sex.



METABOLITE RESULTS

EXPANDED

Uridine

HIGHER RATES ASSOCIATED WITH IMPROVED OMIC AGE

0.02

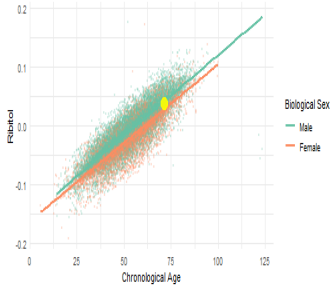
Your **Uridine** is higher than **59.68%** of the population at your same calendar age and sex.

Ribitol

LOWER RATES ASSOCIATED WITH IMPROVED OMIC AGE

0.03

Your **Ribitol** is higher than **51.34%** of the population at your same calendar age and sex.

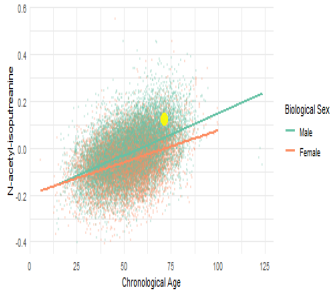


N-acetyl-isoputreanine

LOWER RATES ASSOCIATED WITH IMPROVED OMIC AGE

0.12

Your **N-acetyl-isoputreanine** is higher than **82.01%** of the population at your same calendar age and sex.

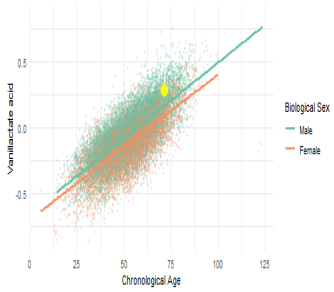


Vanillactate acid

LOWER RATES ASSOCIATED WITH IMPROVED OMIC AGE

0.28

Your **Vanillactate acid** is higher than **85.57%** of the population at your same calendar age and sex.

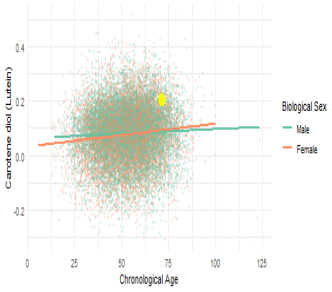


Carotene-3,3-diol (Lutein)

HIGHER RATES ASSOCIATED WITH IMPROVED OMIC AGE

0.2

Your **Carotene-3,3-diol (Lutein)** is higher than **88.53%** of the population at your same calendar age and sex.

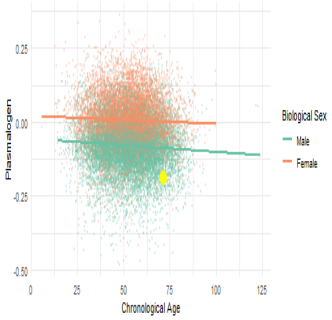


1-stearoyl-2-adrenoyl-GPC (18:0/23:4) (Plasmalogen)

HIGHER RATES ASSOCIATED WITH IMPROVED OMIC AGE

-0.18

Your **1-stearoyl-2-adrenoyl-GPC (18:0/23:4) (Plasmalogen)** is higher than **6.95%** of the population at your same calendar age and sex.

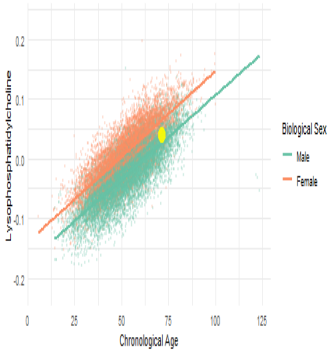


Lysophosphatidylcholine (1-margaroyl-GPE (17:0)*)

LOWER RATES ASSOCIATED WITH IMPROVED OMIC AGE

0.04

Your **Lysophosphatidylcholine (1-margaroyl-GPE (17:0)*)** is higher than **53.95%** of the population at your same calendar age and sex.

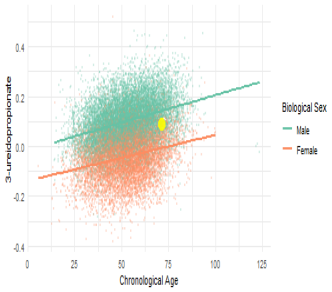


3-ureidopropionate

LOWER RATES ASSOCIATED WITH IMPROVED OMIC AGE

0.08

Your **3-ureidopropionate** is higher than **48.82%** of the population at your same calendar age and sex.

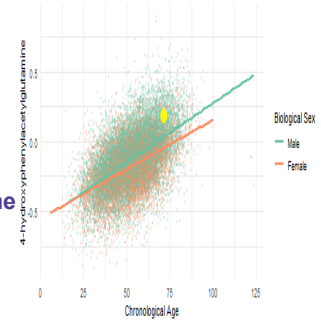


4-hydroxyphenylacetylglutamine

LOWER RATES ASSOCIATED WITH
IMPROVED OMIC AGE

0.18

Your **4-hydroxyphenylacetylglutamine** is higher than **82.62%** of the population at your same calendar age and sex.

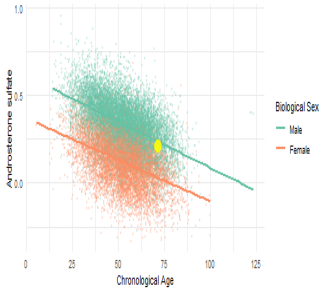


Androsterone Sulfate

HIGHER RATES ASSOCIATED WITH
IMPROVED OMIC AGE

0.21

Your **Androsterone Sulfate** is higher than **60.2%** of the population at your same calendar age and sex.



Phenylacetylglutamine (PAGln)

LOWER RATES ASSOCIATED WITH
IMPROVED OMIC AGE

0.14

Your **Phenylacetylglutamine (PAGln)** is higher than **88.96%** of the population at your same calendar age and sex.

Cystine

LOWER RATES ASSOCIATED WITH
IMPROVED OMIC AGE

0.01

Your **Cystine** is higher than **49.86%** of the population at your same calendar age and sex.

Gluconate

LOWER RATES ASSOCIATED WITH
IMPROVED OMIC AGE

0.09

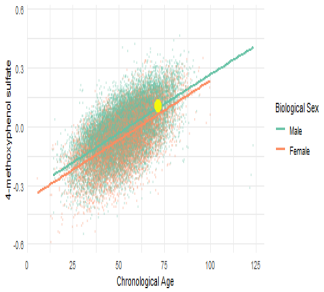
Your **Gluconate** is higher than **83.84%** of the population at your same calendar age and sex.

4-methoxyphenol sulfate

LOWER RATES ASSOCIATED WITH
IMPROVED OMIC AGE

0.1

Your **4-methoxyphenol sulfate** is higher than **57.16%** of the population at your same calendar age and sex.



PROTEIN RESULTS

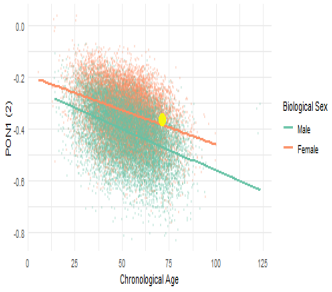
EXPANDED

Serum paraoxonase/ arylesterase

HIGHER RATES ASSOCIATED WITH IMPROVED OMIC AGE

-0.36

Your **Serum paraoxonase/ arylesterase** is higher than **73.5%** of the population at your same calendar age and sex.



Carboxypeptidase B2 (CPB2 or thrombin-activatable fibrinolysis inhibitor)

HIGHER RATES ASSOCIATED WITH IMPROVED OMIC AGE

-0.26

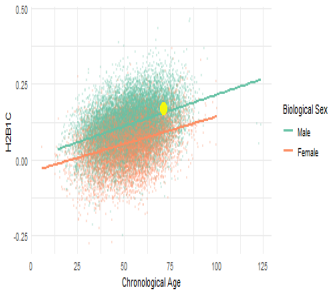
Your **Carboxypeptidase B2 (CPB2 or thrombin-activatable fibrinolysis inhibitor)** is higher than **22.76%** of the population at your same calendar age and sex.

Histone H2B type 1-K

LOWER RATES ASSOCIATED WITH IMPROVED OMIC AGE

0.16

Your **Histone H2B type 1-K** is higher than **70.19%** of the population at your same calendar age and sex.

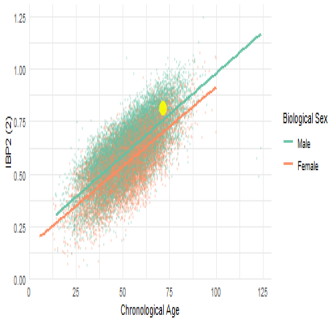


Insulin-like growth factor-binding protein 2

LOWER RATES ASSOCIATED WITH IMPROVED OMIC AGE

0.81

Your **Your Insulin-like growth factor-binding protein 2** is higher than **75.15%** of the population at your same calendar age and sex.

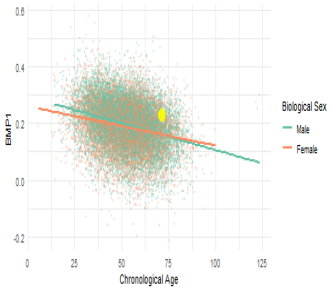


Bone morphogenetic protein 1

HIGHER RATES ASSOCIATED WITH IMPROVED OMIC AGE

0.22

Your **Bone morphogenetic protein 1** is higher than **82.36%** of the population at your same calendar age and sex.

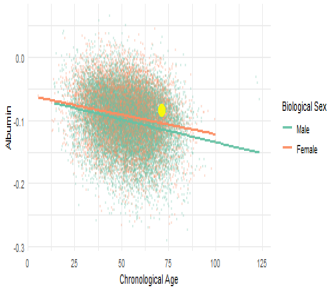


Albumin

HIGHER RATES ASSOCIATED WITH IMPROVED OMIC AGE

-0.08

Your **Albumin** is higher than **71.24%** of the population at your same calendar age and sex.

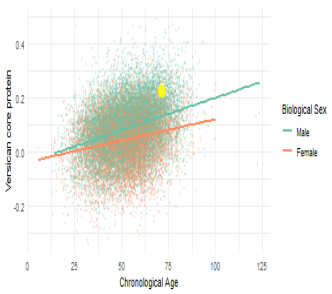


Versican core protein

LOWER RATES ASSOCIATED WITH IMPROVED OMIC AGE

0.22

Your **Versican core protein** is higher than **88.96%** of the population at your same calendar age and sex.

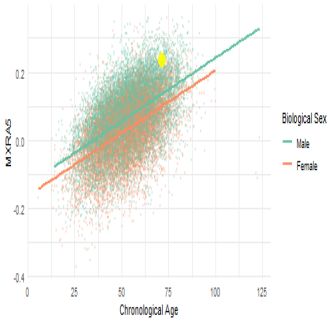


Matrix-remodeling -associated protein 5

LOWER RATES ASSOCIATED WITH IMPROVED OMIC AGE

0.23

Your **Matrix-remodelingassociated protein 5** is higher than **93.39%** of the population at your same calendar age and sex.

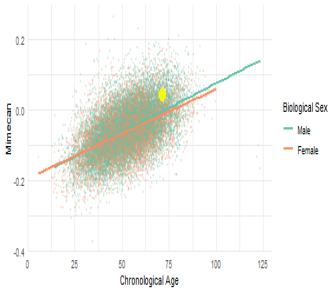


Mimecan

LOWER RATES ASSOCIATED WITH
IMPROVED OMIC AGE

0.04

Your **Mimecan** is higher than **81.92%** of the population at your same calendar age and sex.



Inter-alpha-trypsin inhibitor heavy chain H3

LOWER RATES ASSOCIATED WITH
IMPROVED OMIC AGE

0.6

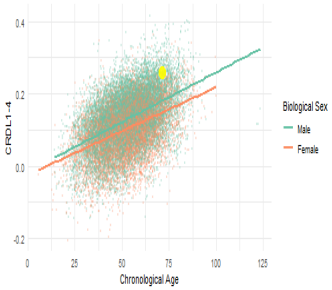
Your **Inter-alpha-trypsin inhibitor heavy chain H3** is higher than **87.14%** of the population at your same calendar age and sex.

CRDL 1-4 protein

LOWER RATES ASSOCIATED WITH
IMPROVED OMIC AGE

0.25

Your **CRDL 1-4 protein** is higher than **91.31%** of the population at your same calendar age and sex.

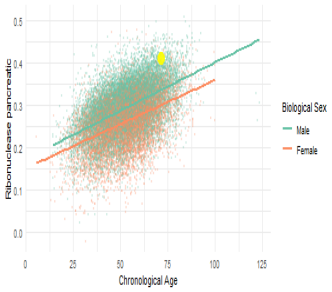


Ribonuclease pancreatic

LOWER RATES ASSOCIATED WITH
IMPROVED OMIC AGE

0.4

Your **Ribonuclease pancreatic** is higher than **95.22%** of the population at your same calendar age and sex.

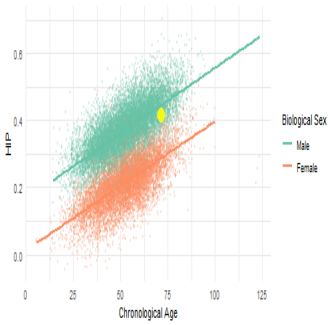


HSP70 interacting protein (HIP)

LOWER RATES ASSOCIATED WITH
IMPROVED OMIC AGE

0.41

Your **HSP70 interacting protein (HIP)** is higher than **53.95%** of the population at your same calendar age and sex.



VALUES FACTORED IN OMICm AGE

Biomarker definitions.

Hemoglobin

Red blood cells contain the protein hemoglobin, which transports oxygen. How much hemoglobin is in your blood is determined by the hemoglobin test. The most significant part of red blood cells is hemoglobin. It is made up of heme, a protein that binds oxygen.

Hematocrit

The volume percentage of red blood cells in blood is assessed as part of a blood test and is referred to by a number of other names. Red blood cell quantity and size determine this measurement.

Creatinine

Creatinine is a waste product that comes from the normal wear and tear on muscles of the body. Everyone has creatinine in their bloodstream. However, amounts vary based on age, body size, race, and gender.

Triglycerides

Triglycerides are a type of fat, called lipid, that circulate in your blood. They are the most common type of fat in your body. Triglycerides come from foods, especially butter, oils, and other fats. Unused calories are stored as triglycerides in fat cells. When your body needs energy, it releases the triglycerides. High triglyceride levels in your blood can raise your risk of heart disease and stroke.

Alkaline Phosphatase (ALP)

Your body contains an enzyme called alkaline phosphatase (ALP). One of the tests in a full metabolic panel, ALP blood tests evaluate the amount of ALP produced by your liver and bones in your blood. High blood levels of ALP may be a sign of liver disease or specific bone problems.

Fasting Glucose

The primary sugar present in your blood is glucose. It serves as the main energy source for your body. It originates in the food you consume. The majority of that meal is converted by your body into glucose, which is then released into your bloodstream. Your pancreas releases insulin when your blood glucose levels rise.

HbA1c

The A1C test, sometimes called a HbA1c test or a hemoglobin A1C test, is a quick blood test that gauges your average blood sugar levels over the previous three months. The primary test to assist you and your healthcare team in managing your diabetes, it is one of the often utilized tests to diagnose prediabetes and diabetes.

Blood Urea Nitrogen (BUN)

The amount of urea nitrogen in your blood is determined by a blood urea nitrogen (BUN) test. When your liver breaks down protein, urea nitrogen is produced as a waste product. Your blood carries it, your kidneys filter it out, and your urine excretes it from your body.

Red Blood Cell Width

The measure of the difference in the volume and size of your red blood cells (erythrocytes). The volume of red blood cells varies even in healthy blood, with an average volume of 80–100 femtoliters. However, some illnesses result in a markedly greater fluctuation in cell size. Greater size variation is indicated by higher RDW values. RDW-CV in human red blood cells typically falls between 11.5 and 15.4%.

Albumin (Clinical)

The protein albumin is produced by your liver. Albumin enters your bloodstream and aids in preventing fluid from seeping into other tissues from your blood vessels. It also transports vitamins, enzymes, and hormones throughout the body. If your blood doesn't contain enough albumin, fluid may leak out and accumulate in your lungs, abdomen, or other areas of your body. Low albumin levels may indicate liver, renal, or other types of illness. Dehydration may be indicated by high levels.

Uridine

Uridine is an important building block used in the creation of RNA. It may support brain health, synaptic connections, and cholinergic function. A 2018 study identified it as one of 12 metabolites predictive of living over the age of 85 in women. Other studies have also shown that it is linked to all-cause mortality. Lower uridine levels in Alzheimer's disease (AD) were associated with clinical progression. In some studies, it has been identified as a factor that promotes human stem cell activity and enhanced regeneration in multiple tissues across multiple mammal species.

Carotene-3,3-diol (Lutein)

Carotene-3,3-diol is one of 600 known naturally occurring carotenoids. It is synthesized only by plants and is found in high quantities in green leafy vegetables such as spinach, kale, and yellow carrots. Some studies have shown that supplementation can help improve cognitive function and eye health. A large meta-analysis involving 71 published papers and representing more than 387,000 individuals showed that people with higher lutein intake, or higher blood concentrations of lutein, have a reduced risk of coronary heart disease, stroke, and metabolic syndrome. Lutein provides such wide-reaching effects because it protects tissues from oxidative stress and inflammation—two factors that play a significant role in cardiovascular and metabolic diseases.

Ribitol

Ribitol is a pentose alcohol formed by the reduction of riboseforms part of the chemical structure of riboflavin and flavin mononucleotide (FMN). It is also a metabolic end product formed by reducing ribose in human fibroblasts and erythrocytes. It has been a blood-based biomarker of diabetic retinopathy and biological process clustering studies have shown it to be associated with insulin secretion and diabetes pathways which are highly related to mortality. Higher concentrations of similar metabolites like ribonic acid have also been linked to CKD.

1-stearoyl-2-adrenoyl-GPC (18:0/23:4) (Plasmalogen)

This is a choline ether phospholipid (ePC) that is present in human serum or plasma. Decreases in ether phospholipids (plasmalogens) in serum (plasma) have been reported in several diseases such as Alzheimer's disease, Parkinson's disease, metabolic syndrome, and schizophrenia.

N-acetyl-isoputreanine

Isoputreanine belongs to the class of organic compounds known as gamma amino acids and derivatives.

Gluconate

Gluconic acid occurs naturally in fruit,honey, and wine . It has been identified as a lifestyle-related biomarker that may be a target to reduce stroke risk in Black adults. Higher levels of gluconic acid in the blood were associated with high blood pressure and increased risk of ischemic stroke among Black adults when compared to white adults. It also may be considered as a dietary-related oxidative stress marker due to its availability in food, potentially produced by the gut microbiome, and related to diseases with oxidative stress. Of the 162 metabolites measured in one study, elevated levels of gluconic acid were found in Black adults who had high blood pressure but not their white peers with high blood pressure. Black adults with the highest gluconic acid levels were 86% more likely to have high blood pressure. Black adults with the highest gluconic acid levels had a 53% increased risk of ischemic stroke. No such association was found for white participants. Gluconic acid accounted for 25% of the association between high blood pressure and stroke among Black adults. After adjusting for multiple factors, a higher level of gluconic acid was associated with a Southern diet (foods high in added fats, fried foods, processed meats, and sugary drinks), and a lack of exercise.

Phenylacetylglutamine (PAGln)

Phenylacetylglutamine (PAGln) is a gut microbiota-derived metabolite that may induce cardiovascular events by activating platelets and increasing the risk of thrombosis. The highly-nitrogenous compound is most commonly encountered in human subjects with urea cycle disorders. These conditions, such as uremia or hyperammonemia, tend to cause high levels of nitrogen in the form of ammonia in the blood. It also has been used as a biomarker of acute stroke. High levels of phenylacetylglutamine in the urine following metabolism by the gut microbiota may also indicate early renal decline associated with kidney dysfunction and chronic kidney disease (CKD). In CKD, phenylacetylglutamine is considered a uremic toxin which is taken up, circulated, and retained in the blood after microbial fermentation of certain proteins and amino acids in the gut. Blood serum levels of phenylacetylglutamine in CKD are used as a mortality determinant. Blood plasma levels of phenylacetylglutamine increase with exposure to cigarette smoke, in patients with ischemic heart failure, with cardiovascular risk or hypertension, in patients with disease, and in patients with type 2 diabetes.

Serum paraoxonase/arylesterase

Serum paraoxonase and arylesterase 1 (PON1) is an enzyme encoded by the PON1 gene. Serum PON1 is secreted mainly by the liver, although local synthesis occurs in several tissues and PON1 protein is found in almost all tissues. PON1 is also a major anti-atherosclerotic component of HDL Cholesterol (good cholesterol). The PON1 gene is activated by PPAR-γ, which increases synthesis and release of paraoxonase 1 enzyme from the liver, reducing atherosclerosis. In addition to protecting against exposure to some organophosphorus (OP) pesticides by hydrolyzing their toxic oxon metabolites, PON1 is important in protecting against vascular disease by metabolizing oxidized lipids. Circulating plasma levels of leptin, hs-CRP, and IL-6 were significantly non-linearly associated with arylesterase activity. Leptin levels were also significantly associated with paraoxonase activity independently from confounding factors, including high-density lipoprotein (HDL) cholesterol. With increasing levels of inflammatory parameters, arylesterase, and paraoxonase activities increased; This suggests that in persons with very high levels of inflammation, PON1 activity may be impaired, a fact that might subsequently be accompanied by a higher risk for cardiometabolic diseases.

Lysophosphatidylcholine (1-margaroyl-GPE (17:0)*)

Lysophosphatidylcholine (LPC) is increasingly recognized as a key marker/factor positively associated with cardiovascular and neurodegenerative diseases. LPC is mainly derived from the turnover of phosphatidylcholine (PC) in circulation by phospholipase A2 (PLA2). In the presence of Acyl-CoA, lysophosphatidylcholine acyltransferase (LPCAT) converts LPC to PC. However, overexpression or enhanced activity of PLA2 increases the LPC content in modified low-density lipoprotein (LDL) and oxidized LDL, which play significant roles in the development of atherosclerotic plaques and endothelial dysfunction. Hydrolysis of LPC by autotaxin, an enzyme with lysophospholipase D activity, generates lysophosphatidic acid, which is highly associated with cancers.

Vanillactic acid

Vanillactic acid, also referred to as vanillactate or VLA falls within the category of organic substances termed phenylpropanoic acids. Phenylpropanoic acids are compounds characterized by a structure that incorporates a benzene ring connected to propanoic acid. Vanillactic acid possesses potential toxicity and has been associated with inborn metabolic disorders, including aromatic l-amino acid decarboxylase deficiency.

3-ureidopropionate

Ureidopropionic acid is essentially a urea derivative of beta-alanine. High levels of ureidopropionic acid are found in individuals with beta-ureidopropionase (UP) deficiency. It has been identified as one of the major metabolites Metabolites Associated With the Risk of Developing Mobility Disability This can also be present in Albuminuria. Albuminuria is an indicator of sub-clinical organ damage and a marker of cardiovascular risk and renal disease.

4-hydroxyphenylacetylglutamine

4-Hydroxyphenylacetylglutamic acid belongs to the class of organic compounds known as glutamic acid and derivatives. This is a metabolite which is upregulated in cystic fibrosis. It also has been suggested to be a novel biomarker of type 2 diabetes with polyneuropathy and also has shown a link to systolic blood pressure in women.

Cystine

Cystine (Cys) the primary sulfur-containing amino acid (SAA) is a semiessential amino acid (AA) because it can be obtained from the diet or produced from methionine degradation via the transsulfuration pathway. Cystine is common in many foods such as eggs, meat, dairy products, and whole grains as well as skin, horns, and hair. Within the body, cystine catabolic pathways are sources of the synthesis of coenzyme A, glutathione, taurine, and oxidized and reduced inorganic sulfur. Cystine is more easily absorbed by the body than cystine, so most supplements contain cystine rather than cystine.

Androsterone Sulfate

Androsterone sulfate (Andros-S) is the most abundant 5-alpha-reduced androgen metabolite in serum. This means higher testosterone levels generally yield higher versions of this metabolite.

Bone morphogenetic protein 1

Bone morphogenetic protein 1, also known as BMP1, is a protein that in humans is encoded by the BMP1 gene. It induces bone and cartilage development. BMP-1 stimulates the conversion of newly secreted proapo A1 to its phospholipid- (PL-) binding form. In this way, it promotes the formation of functional HDL and reverse cholesterol transport. Higher levels of inflammation have been shown to be associated with a decrease in BMP1 and therefore APOA1 and thus it has been suggested as a marker for inflammation and cardiovascular disease risk.

Carboxypeptidase B2 (CPB2 or thrombin-activatable fibrinolysis inhibitor)

CPB2 is synthesized by the liver and circulates in the plasma as a plasminogen-bound zymogen. When it is activated by the thrombin/thrombomodulin complex, CPB2 exhibits carboxypeptidase activity. Activated CPB2 reduces fibrinolysis by removing the fibrin C-terminal residues that are important for the binding and activation of plasminogen. Lower CPB2 has been suggested as a biomarker of peripheral artery disease. This could be a biomarker of chronic hepatitis and thrombotic risk. Profound hypercoagulability seems to be mediated by the overexpression of plasminogen activator inhibitor 1 (PAI-1) and CBP2.

Albumin

The protein albumin is produced by your liver. Albumin enters your bloodstream and aids in preventing fluid from seeping into other tissues from your blood vessels. It also transports vitamins, enzymes, and hormones throughout the body. If your blood doesn't contain enough albumin, fluid may leak out and accumulate in your lungs, abdomen, or other areas of your body. Low albumin levels may indicate liver, renal, or other types of illness. Dehydration may be indicated by high levels.

Histone H2B type 1-K

Histone H2B type 1-K is a core component of the nucleosome or the proteins which wrap and control the expression of DNA. Nucleosomes wrap and compact DNA into chromatin, limiting DNA accessibility to the cellular machinery which requires DNA as a template. Histones thereby play a central role in transcription regulation, DNA repair, DNA replication, and chromosomal stability. DNA accessibility is regulated via a complex set of post-translational modifications of histones, also called histone code, and nucleosome remodeling. H2B Type 1-K has been shown to accumulate in senescent Fibroblasts with Persistent DNA Damage.

Versican core protein

Versican is an extracellular matrix protein that has been shown to increase during inflammation in a number of different diseases such as cardiovascular and lung disease, autoimmune diseases, and several different cancers. Versican interacts with inflammatory cells either indirectly via hyaluronan or directly via receptors such as CD44, P-selectin glycoprotein ligand-1 (PSGL-1), and toll-like receptors (TLRs) present on the surface of immune and non-immune cells. These interactions activate signaling pathways that promote the synthesis and secretion of inflammatory cytokines such as TNFα, IL-6, and NFκB.

Insulin-like growth factorbinding protein 2

IGFBP-2 is an insulin-like growth factor (IGF) binding protein (IGFBPs) that modulates IGF-I's actions. It plays an important role in the regulation of several cellular processes. IGFBP-2 is the second most abundant IGFBP and is expressed in several tissues, including blood vessels and the skeleton. IGFBP-2 can prevent IGF-I binding to its receptor, but it also modulates cellular functions independently of IGF-I binding It has been suggested to be a biomarker of metabolic disease and diabetes.

Matrix-remodeling-associated protein 5

This gene encodes one of the matrix-remodeling associated proteins. MMPs are capable of degrading all kinds of extracellular matrix proteins but also can process a number of bioactive molecules. They are known to be involved in the cleavage of cell surface receptors, the release of apoptotic ligands, and chemokine/ cytokine inactivation. MMPs are also thought to play a major role in cell behaviors such as cell proliferation, migration (adhesion/dispersion), differentiation, angiogenesis, apoptosis, and host defense.

Mimecan

Mimecan, also known as osteoglycin, is an ECM component. Mimecan affects several biological processes including the regulation of collagen fibrillogenesis and angiogenesis. Mimecan is expressed in atherosclerotic tissue and Human coronary arteries and is downregulated in intimal vascular smooth muscle cells (VSCMs). Studies have shown mimecan is associated with a vulnerable plaque phenotype, possibly regulated by plaque inflammation, and thus might predict future cardiovascular death and arterial stiffness.

Ribonuclease pancreatic

Pancreatic ribonuclease also known as ribonuclease A (RNase A) or ribonuclease 1 (RNase1) is an enzyme that catalyzes the breakdown of RNA and plays a role in the digestion of RNA in vertebrate species. RNase is present in much lower amounts in humans than in other species and may account for only 0.5 to 1% of pancreatic enzymes. Although only a few studies exist, pancreatic RNase in all species appears to break down dietary nucleic acid in the gut lumen to nucleotides. Not much is described about this protein as a biomarker, however, highway levels have been linked to more aggressive cancers.

Inter-alpha-trypsin inhibitor heavy chain H3

Inter-alpha (globulin) inhibitor 3 (ITIH3), one of the constituents of plasma serine protease inhibitors, has been shown to be related to the proinflammatory process (Fries and Kaczmarczyk 2003). This complex, named pre-alpha trypsin inhibitor (PαI) is synthesized by hepatocytes and released to the blood vessel upon stimulation of the proinflammatory cytokines (tumor necrosis factor or interleukin-1). Then, ITIH3 makes a complex with the locally synthesized hyaluronan (HA) and interacts with inflammatory cells (Fries and Kaczmarczyk 2003). - ITIH3-HA complex has been reported to be involved in inflammatory diseases, including rheumatoid arthritis and inflammatory bowel diseases (Zhuo et al. 2004). Variants with this protein have also been shown to be associated with psychiatric diseases.

HSP70 interacting protein (HIP)

HSP90 interacting protein is a co-chaperone heat shock protein that helps with appropriate protein folding. One aspect of this protein, C terminus of Hsc70-interacting protein (CHIP), frequently promotes ubiquitination and degradation of several proteins. The impact of upregulated CHIP has not been well studied. CHIP has been reported to play an important role in preventing cell apoptosis. CHIP also displays a critical cardioprotective effect in response to ischemia/reperfusion injury. CHIP is a negative regulator of FoxO1 activity through ubiquitin-mediated degradation, and inhibition of CHIP has been postulated to serve as a potential therapeutic target for reducing proliferative arterial diseases.

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