CERASCREEN WHITE PAPER SERIES

Longevity – Introduction to an epigenetic lifestyle and diet

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We think that we are who we are because of the genes we inherited from our parents. But novel research reveals that we are who we are not only because of the genes we received from our parents, but also because of the environment in which we, our parents and our grandparents lived.

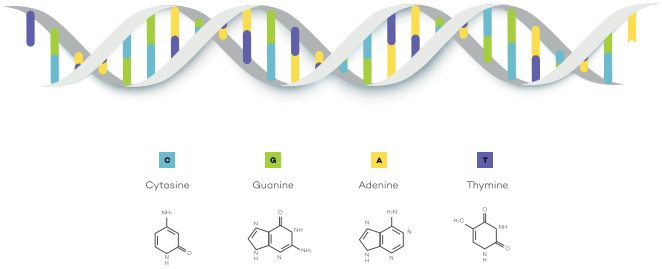
Therefore, it's not ALL in the genes - external and environmental factors can influence the way our genes are regulated. This field of genetics is known as epigenetics - 'epi' a Greek word for 'over / on top of'.

So.. **What is Epigenetics?**

Epigenetics is an additional layer of instructions that lies 'on top of' DNA. This additional layer does not change the DNA sequence, but affects how cells „read" genes i.e. how our DNA turns genes 'on' or 'off'.

Almost every cell in the human body contains a nucleus containing the 23 chromosomes. The chromosomes consist of DNA tightly wrapped around histones. DNA is a complete set of instructions that tells cells what proteins to make. A gene is a short section of DNA.

DNA is a very long molecule, made up of smaller pieces known as nucleotide bases. There are four bases: guanine, cytosine, adenine and thymine. Humans have 3 billion nucleotide bases in their DNA. The sequence of these bases is different between individuals, which is the reason for our being unique.



So, the DNA found in the nucleus of nearly every cell of our body contains all of our genes, plus extra DNA that is required to ensure the genes are properly controlled. Combined, this is known as the genome.

But, how do we end up with all the different cells that make up all the different body parts? We obviously are made up of different cell types, brain cells, heart cells, skin cells, liver cells, and many more. This process is called 'cell differentiation' and is just one example of epigenetics – the extra layer of information lying above the genes and surrounding the DNA tells them which ones to switch on or off, this influences the production of proteins in certain cells, ensuring that only necessary proteins are produced to build each of the different functional cells the body needs. For example, proteins that promote bone growth are not produced in muscle cells. Patterns of epigenetic modification vary among people, different tissues within the individual, and even different cells.

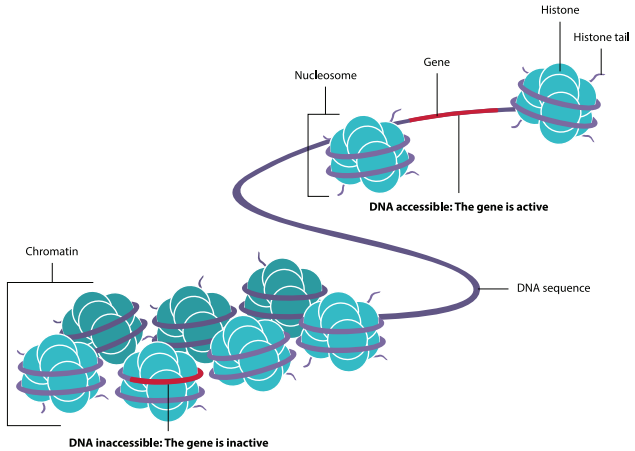
Epigenetic modifications stay as cells divide and in some cases can be inherited through the generations. Environmental influences, such as a person's diet type and exposure to pollutants, can also impact the epigenome.

DNA Methylation

During cell division, the DNA strand is unwound, divided, read and duplicated. This process is controlled by epigenetics. Essentially, there are two instruments for this. The first is histone modification. Histones can be modified by biochemical compounds docking to them and actively promoting or preventing the unwinding of the DNA. DNA can only be read and reproduced in the unwound state.

The second commonly known type of epigenetic modification is direct DNA methylation. DNA methylation is a heritable epigenetic mark, established early in development, and involves the attachment of small molecules called methyl groups (each methyl group consists of one carbon atom and three hydrogen atoms), directly to the segments of DNA. When methyl groups are added to a particular gene, that gene is turned off and no protein is produced from that gene. The DNA section where methyl groups attach most likely are called CpG islands.

Why CpG Islands? The CpG islands are sections of the DNA where the combination of the two bases cytosine (C) and guanine (G) occurs above average or more frequently. To give you an idea about the complexity: There are about 28 million CpG islands in the human genome that regulate the gene activities.



DNA methylation is one of the most studied and stable epigenetic modifications, these modifications have effects on gene function, protein production, and human health. Also, it has been shown to be associated with aging, aging-related health outcomes, and the indicator for all-cause and disease-specific mortality.

Epigenetic Errors

The errors in the epigenetic process, such as modifying the wrong gene or failing to turn a gene 'on' or 'off', can lead to abnormal gene activity or inactivity, causing genetic disorders. Conditions such as: metabolic disorders, degenerative disorders, and cancers have all been found to be related to epigenetic errors.

Cancer is now being recognized as both a genetic and epigenetic disease. The DNA in cancer cells was found to have a different methylation pattern than those of normal healthy cells. The messed up methylation pattern in cancer cells results in the genome being abnormally suppressed or active.

Epigenetics and longevity

Aging is an unavoidable outcome of life, characterized by a progressive decline in organs and tissues functions with an increased risk of mortality. Increasing evidence now is linking aging to genetic and epigenetic alterations, and with the reversible nature of epigenetic mechanisms, this shows a promising future for therapeutics against age-related decline and disease.

Your Lifestyle Impacts your Epigenetics & Longevity...

Obesity & Physical Activity

Overweight, obesity, and a sedentary lifestyle are common risk factors for several diseases, including cardiovascular disease and cancer. Because bodyweight is regulated by genes controlling energy homeostasis, it has been hypothesized that dietary macronutrients that affect DNA methylation could contribute to developing obesity through epigenetic mechanisms.

In a recent study, physical activity was associated with higher methylation in peripheral blood lymphocytes. Interestingly, elderly individuals with high methylation in peripheral blood lymphocytes have been recently shown to have a lower incidence and mortality from ischemic heart disease and stroke.

Exercise

Physical exercise has been shown to decrease and even reverse hypermethylation, lowering the risk of cancer development. Exercising increases levels of eustress, or good stress, on the body. This eustress stimulates epigenetic modifications affecting the DNA genome of cancer cells.

Tobacco smoke

The molecules and tar in tobacco smoke have been proved to have carcinogenic and mutagenic effects. Studies showed that exposure to high-dose of tobacco smoke caused epigenetic downregulation; however, this was restored one week after smoking cessation.

Alcohol

Alcohol acts mainly as a cocarcinogen. A Netherlands study on diet and cancer correlated the intake of alcohol with changes in methylation of tumor suppressor and DNA repair genes.

Also, alcohol consumption at the early stage of pregnancy altered the DNA methylation in embryos with disturbances in the expression of genes involved in metabolism and development. These disturbances may contribute to malformations and abnormal fetal development.

Psychological Stress

Studies have indicated that DNA methylation is sensitive to environmental stressful exposures in early development and later in life.

Shift Work

The so-called CLOCK gene may be affected by different factors such as shift-work. According to several studies, shift-work that requires working at night can have a negative impact on the health and well-being of workers due to a mismatch between the endogenous timing system and the environmental synchronizers (e.g. light/dark cycle). Epigenetic reprogramming of endogenous timing genes has been proposed as a potential response. A recent study on a population of night-shift workers has shown alterations in blood DNA methylation, and gene-specific methylation of inflammatory genes.

Air Pollution

Air pollution negatively affects your DNA. The fine particles with a diameter of less than 2.5 micrometers have been shown to damage the epigenetic on your DNA, increasing your chances of a stroke, Alzheimer's disease, Parkinson's disease, cognitive impairments, and neurodevelopmental disorders. In fact, hundreds of genes can be affected by inhaling the widespread air pollutants. One example of a common air pollutant is the diesel exhaust fumes. Diesel exhaust arises when engines burn diesel fuel, this exhaust (known as soot) is a complex mixture of thousands of gases and fine particles. This soot contains more than 40 toxic air contaminants many of which are cancer-causing substances, such as benzene, arsenic and formaldehyde.

Previous studies have found that breathing in diesel fuel exhaust fumes can lead to changes in DNA methylation, switching on and off certain genes.

In a study investigating the epigenetic changes and DNA methylation between two groups – the first was exposed to the diesel exhaust fumes and the second group was exposed to only filtered air.

They found that only two hours of exposure to diesel exhaust fumes was long enough to have an impact on DNA methylation. The group who was exposed to diesel exhaust had 2,827 different points on their DNA differentially methylated, and this affected around 400 genes. These changes show how sensitive the genes can be to harmful chemicals, especially air pollution, and that harmful changes can occur even without noticeable symptoms. Asthma, higher blood pressure, or arrhythmia might just be the gradual accumulation of these epigenetic changes.

Fortunately, changes that happen so quickly can probably be reversed, either through therapy, change in environment, and change in lifestyle, or diet.

Nutrition & Epigenetics: The future

Nutrition conditions (e.g. high-calorie diets, calorie restriction), nutrients and bioactive food components (a type of chemical found in small amounts in plants and certain foods such as; fruits, vegetables, nuts, oils, and whole grains) can reverse or change the epigenetics (DNA methylation status, histone modifications, and chromatin remodeling), and subsequently altering gene expression and having an impact on overall health. Diet and lifestyle factors modify DNA methylation age assessed by the epigenetic clock, and therefore may be able to slow epigenetic aging.

Bioactive food components, specific nutrients, and dietary patterns may have beneficial effects and overcome the negative impact of negative lifestyle, such as smoking or exposure to certain chemicals and pollution. Yet, nutritional epigenetics is a quite recent subfield of epigenetics, and the available data is limited. A recent study showed that fruit and juice epigenetic signatures as measured by DNA methylation marks are associated with independent immunoregulatory pathways, suggesting that the health benefits of fruit and juices are distinct.

The high-calorie diet may adversely change DNA methylation profile, while calorie restriction without malnutrition slows aging and prevents cancer. Calorie restriction affects methylation and regulates metabolism, inflammation and lifespan.

We gathered the latest findings and knowledge regarding nutritional epigenetics, which will be helpful for an understanding of how nutrients contribute to our health.

Vitamin B2, B3, B6, B9 and B12

B Vitamins appeared to positively influence the epigenetic pattern and can help decrease your epigenetic age. Studies found that after 2 years of supplementation with B vitamins improved methylation was observed in participants, especially women. The researchers speculated that men may need more vitamin B9 to see benefits because of their greater body mass.

Also, it is assumed that including these vitamins B2, B3, B6, and B12 in diets may contribute to the maintenance of DNA methyl marks and therefore regulate DNA methylation.

A recent study showed that taking B-vitamin supplementation (2.5 mg of folic acid B9, 50 mg vitamin B6, and 1 mg vitamin B12) was able to prevent the harmful effects of air pollution on DNA methylation.

These B vitamins can be found naturally in many food:

Vitamin B2

- Beef
- Oats
- Yogurt
- Milk
- Clams
- Mushrooms
- Almonds

Vitamin B6

- Chickpeas
- Dark Leafy Greens
- Poultry
- Beef Liver
- Salmon and Tuna

Vitamin B12

- Fish
- Liver
- Red Meat
- Poultry
- Eggs
- Fortified Milk, Cereals, and nutritional yeast

Vitamin B3

- Beef Liver
- Chicken
- Salmon and Tuna
- Brown and White Rice
- Peanuts

Vitamin B9

- Dark Leafy Greens
- Peanuts
- Beans
- Seafood
- Sunflower Seeds
- Eggs

Calcium

The most abundant mineral in the human body, it is mostly found in the bones (98–99%) and cells (1–2%). The main functions of calcium include its import role during blood coagulation as well as growth and mineralization of skeletal muscle. Calcium has been suggested to reverse epigenetic silencing (switching-off) of tumor suppressor genes in colonic cancer. Coincidingly, calcium deficiency was connected to hypo-methylation. Yet, the underlying mechanisms need to be explored more deeply.

Calcium is naturally available from a wide variety of foods, added to fortified food, available as a supplement, and contained in certain medications. The recommended daily allowance for both men and women is 1000 milligrams.

Milk
300 mg per 1 cup

Salmon (with bones)
241 mg per 4 ounces

Sardines (with bones)
213 mg per 2 ounces

Spinach, cooked
145 mg per 1/2 cup

Almonds
93 mg per 1/2 cup

Orange
52 mg per medium orange

Mushrooms
18 mg per 2 ounces

Zinc

Zinc (Zn) is an essential micronutrient element for the body as it plays a key role in a variety of biological activities, including epigenetic regulations. Accumulating evidence has demonstrated that zinc plays an important role in DNA methylation and that zinc deficiency may lead to epigenetic dysregulation.

Studies showed that zinc deficiency was linked to increased chronic inflammation, especially in elderly people, with subsequent alteration in the DNA methylation status of the genes involved in inflammation.

This chronic low-grade inflammation occurring in the absence of overt infection has been known as "inflammaging" and represents a significant risk factor for morbidity and mortality in the elderly.

A zinc-rich diet might help keep away the "inflammaging". The recommended daily zinc intake is 8 and 11 milligrams for women and men, respectively. It is suggested that these recommendations may need to be adjusted when applied to elderly individuals to ensure they are receiving a sufficient amount of zinc.

Zinc dietary sources include:

- Seafood, such as oysters, crab and lobster
- Turkey
- Beans
- Chickpeas
- Nuts
- Pumpkin seeds
- Whole grains
- Milk
- fortified Cereals
- Cashews

Because a vegetarian diet provides lower zinc amounts than an omnivorous diet, vegetarians may need to double their intake of zinc-rich foods.

Selenium

Selenium may have anticarcinogenic properties through modifications of epigenetic processes in the cell and can also restore the expression of hypermethylated genes in human prostate cancer cells. Moreover, in animal models, a selenium-deficient diet has been shown to induce DNA hypomethylation. Foods high in selenium include Brazil nuts, tuna, oysters, pork, beef, chicken, tofu, whole wheat pasta, shrimp, and mushrooms. The recommended daily value for selenium is 55µg (micrograms).

Curcumin

Curcumin, a component of the golden spice Curcuma longa, commonly known as turmeric, has recently been determined to have the potential to regulate epigenetics.

Research shows that curcumin can epigenetically regulate the expression of important genes by reversing DNA methylation and altering histone modifications and by targeting several miRNAs that play a key role in several diseases. These findings suggest that curcumin might be a promising agent to treat various human diseases that can occur due to alterations in epigenetics, including cancers.

Curcumin is fat-soluble, so if you take regular curcumin with just water, your body will only absorb very little amount. Therefore, it is best to be taken with a fatty meal. In addition, curcumin does not stay in the body for a long time, so, to keep curcumin levels in your body up, it is advised to take curcumin twice daily.

Tip: Black pepper enhances curcumin absorption in the body by up to 2000%. So, to get the most out of your curcumin, add 3% ground black pepper to your curcumin powder, which is about 1/2 teaspoon of ground pepper to every 1/4 cup of curcumin powder.

If you're wondering how to incorporate curcumin into your diet, here are some ways to eat or drink this spice.

+ Try adding a pinch of curcumin to scrambled eggs or a delicious frittatas dish.
+ Toss it with roasted vegetables, such as cauliflower or potatoes for a warm spicy flavor.
+ Adding a pinch of curcumin to a pot of plain rice will add color and a nice warm flavor.
+ Sprinkle some curcumin into salads or sautéed leafy greens.
+ Add some to a bowl of chicken or vegetable soup.
+ Blend it into your favorite smoothie.
+ Maybe it's time to try the "Golden Milk" beverage that has been gaining popularity lately. Simmer curcumin with (cow's, almond, or coconut) milk and add some honey to make an earthy and comforting beverage. You can also add vanilla extract, coconut oil, cinnamon, or ginger powder.

Resveratrol

Resveratrol is one of a group of compounds called polyphenols. It has antioxidant properties that protect the body against damage. It is thought to possibly help with longevity, anti-inflammation, healthy-heart, and anti-cancer properties through a variety of mechanisms.

Plants are known to synthesize resveratrol as part of the defense mechanism in response to environmental stress including water deprivation, ultraviolet (UV) irradiation, and especially fungal infection.

Resveratrol is abundant in the skin of red grapes, and in berries, such as blueberries and cranberries, raspberries, and mulberries, and cacao beans, peanuts, and pistachios. It is also found in significant concentrations in red wine.

While all red grapes contain resveratrol in their skins, purple or red grapes, as well as grapes from cooler regions, contain a higher concentration than thin-skinned white or green grapes, or grapes from warmer countries. Thick-skinned Malbec or muscadine grapes have the highest concentration of all. Resveratrol is also found in the seeds, stems, and leaves of the grapevines.

The skins of grapes contain about 50–100 mg resveratrol and are believed to contribute to the cardioprotective abilities of red wine, which contains about 0.2–7 mg resveratrol per liter of the wine. Many studies have described promising health benefits associated with wine consumption, these beneficial effects are due to resveratrol present in red wine. Some studies suggest that red wine is more cardioprotective than white wine.

Resveratrol treatment was linked to cell cycle, proliferation, and apoptosis. Besides, studies have shown that resveratrol reverted epigenetic and transcription changes induced by cigarette smoke in rats. Studies also showed that mild to moderate

alcohol consumption has been associated with a reduced incidence of morbidity and mortality from coronary heart disease.

Resveratrol is now referred to as 'Rejuvenating Resveratrol' or 'Miracle molecule' as it reduces the impact of free radicals that cause aging. Also, it prevents high fat-accelerated aging.

Amaranth Grain

Gluten-Free, protein, minerals, and vitamins rich grain full of benefits, they have been recognized as complete food due to their excellent essential nutrients especially the amino acid balance and a load of phytochemical nutrients. All these compounds possess more health benefits beyond just the high nutritional value, especially the antioxidant and anti-inflammatory properties, which are crucial in reducing the risk of oxidative stress-related chronic diseases including cancer, cardiovascular diseases, diabetes, obesity, and aging. Future research is needed for identifying.

Amaranth bioactive components related to their epigenetic beneficial effects and the mechanisms of such effects.

Amaranth also helps keep your digestive system regulated, make you stronger, and reduce the risk of fracture or broken bones

Minerals	Amaranth (per 100g)
Calcium	159 mg
Copper	0,53 mg
Iron	7,61 mg
Magnesium	248 mg
Manganese	3,33 mg
Phosphorus	577 mg
Potassium	508 mg
Sodium	4 mg
Zinc	2,87 mg
Selenium	18,7 mcg

Vitamins	
Ascorbic acid	4,20 mg
Riboflavin	0,20 mg
Folate	82 mcg
Niacin	0,92 mg
Thiamin	0,12 mg
Vitamin A	2 IU
Pantotenic acid, Vit. B55	1,46 mg

Adding amaranth to your daily diet can have great benefits. Here are a few ideas about how to include amaranth grain into your diet:

+ Mix amaranth with fruit, nuts, and yogurt for breakfast
+ Make “rice cakes” with amaranth and honey
+ Use amaranth flour to make gluten-free baked goods
+ Add amaranth to soup
+ Serve amaranth instead of rice, pasta, orzo or risotto
+ Make “pudding” with amaranth
+ Add amaranth to your smoothie for a nutty flavor

Betanins / Beets

Betalains are phytonutrients, they give beets their red color. The beetroots and leafy greens are rich in potassium, magnesium, phosphorus, iron, beta-carotene, folic acid, and vitamins A, B and C. The root specifically is the source of all B vitamins as well as potassium, magnesium, iron, and manganese, while, the top the leafy greens offer carotenoid and flavonoid antioxidants, and vitamins C and A. The leafy greens also contain more iron than spinach. Beets are potent antioxidants, anti-inflammatory, and support the detoxification process.

The latest studies showed that betanin has chemoprevention activities that may disrupt carcinogenesis and associated betalains with reducing cancer risk and lessening tumor cell growth. Betanins are 'non-mutagenic' which means they affect mechanisms of transformed cells by reducing their growth rate and mutations and inducing apoptosis (programmed death of damaged cells). Thus, betanins affect both the tumor growth rate and the tumor cell itself.

Betalains are highly concentrated in beet's peel and flesh, however, beets lose it's nutritional value with heat, so to get the most betalain benefit, beets should be steamed for no more than 15 minutes, if at all.

Green Tea

Contains about half the caffeine of black tea, yet with great taste, and many health benefits in every cup. Tea polyphenols are well known for their beneficial health effects. Interestingly, the existing literature show that the majority of the studies are carried out for green tea polyphenols rather than black tea polyphenols despite the fact that black tea is the most commonly consumed form of tea.

Green tea not only has powerful antioxidant effects, but tea polyphenols can help prevent cancer by balancing the normal DNA methylation status and correcting epigenetic mutations that take place in DNA methylation, histone modifications, and micro-RNAs. In other words, 'turn-on' genes that suppress cancer formation, and 'turn-off' genes that induce cancer formation.

A recent study showed that women (not men) who consumed tea had DNA methylation changes in the DNA collected from their blood, which influences the suppression of cancer genes.

Neohesperidin Dihydrochalcone (NHDC)

Sometimes abbreviated to neohesperidin DC or NHDC, is an intensive sweetener obtained by alkaline hydrogenation of neohesperidin extracted from the peel of oranges.

Naturally, NHDC is found in grapefruits.

This sweetener does not raise blood sugar levels in the body and for this reason, diabetics, people sensitive to regular sugar, and those who are trying to shed some extra pounds can eat foods containing it without worry.

High sugar intake not only increases your risk for obesity and cancer, but it might even make you age faster. A study in the Journal of Nutrition, Health, and Aging found that high blood glucose could damage the end caps of our DNA called telomeres, which has been associated with aging. The higher the blood sugar, the more significant the damage was to the telomere and DNA.

The epigenetic beneficial effects of NHDC include anti-inflammation, anti-cancer, and cardiovascular protection activities. NHDC is also a strong antioxidant with a significant free radical scavenging activity, inhibition of hypochlorous acid-induced DNA strand breakage, protein degradation, and cell death.
NHDC is mostly used in the food industry as a sweetener (E959), and to enhance flavor. Currently, it is being used as an alternative to other dangerous sugar substitutes such as cyclamate, aspartame, and saccharin.

It can be found in a wide range of food products instead of crystallized sugar, such as; milk, cream, ice creams, mayonnaise, ketchup, and mustard. It is also used in the production of salami, sausages, in addition to gum, chewable candy, lollipops, breath mints, jelly bonbons, dried fruits, jams, jellies, purees, snacks, cereals, wafers, biscuits and all kinds of baked goods. It can also be found in shakes, juices, nectars, sodas, liqueurs, beer, canned fish, marinades, preserved seafood, mixed pickles, chutneys, compotes, and weight loss food products. In addition to toothpaste and mouthwash ingredients. Neohesperidin dihydrochalcone is used by the pharmaceutical industry as well - in cough syrups, vitamin complexes, lozenges, etc.

In conclusion

Epigenetics is the study of the changes that occur to your DNA due to aging, lifestyle, environmental factors, and stressors you've faced throughout your life. Studies showed that changes in the DNA of your parents or grandparents can also affect your DNA.

Epigenetic patterns can change throughout life. Studies suppose that examining these epigenetic patterns can help determine the person's 'true age,' as opposed to the chronological age associated with the birthdate. The 'true age' also referred to as the 'biological' or 'physiological' age which is dependent on lifestyle, diet, and other factors rather than just the number of years lived. The epigenetic 'true' age of supercentenarians are markedly younger than their chronological ages.

Also, epigenetic patterns can be positively addressed with an active and healthy lifestyle. Especially a healthy nutrition plays a vital role. The fast-growing research base in epigenetics will give birth to a whole new understanding to healthy and smart eating in the upcoming years.

Authors

+ Lamia A. Kader
Medical Doctor and Medical Research Professional

"The epigenetic research community is developing rapidly and their findings have a direct impact on our daily lives."

+ Dr. Wilfried Blum
Chief Scientific Officer cerascreen GmbH

"Epigenetic is such a fascinating part of life science. For the first time, we get insight in the complexity of gene regulation, where environmental conditions might become inheritable. And with the analysis of epigenetic DNA sites we might have the key in our hands to heal or cure many serious diseases "

+ Dr. Sheraz Gul
Head of Drug Delivery, Fraunhofer IME

„The genetic age provides a more precise picture of our aging process than our chronological age ever could. Today, genetic age allows us to identify things that may be affecting aging and do something about it."

+ Dr. Tim Schiederig
Research Team cerascreen GmbH

"Why I am into epigenetics? It is interesting to know how old your own body really is. Today we know that 25% of the average lifetime of a person is determined by genes; 75% of the personal lifestyle. We all age at different speeds and depending on numerous environmental factors."

About cerascreen

cerascreen is the leading European provider for digital healthcare. Its core business is so-called direct-to-consumer test kits, i.e. laboratory tests for private consumers to determine allergies, vitamin deficiency and hormone levels, as well as individual dietary supplements. The results and recommendations from cerascreen enable customers to build up and improve their personal health profile. The cerascreen services are available in 18 European countries.

cerascreen®

THE INTEGRATED HEALTHCARE COMPANY

In 19 countries with over 250.00analyzed tests.

What we have done so far

1000+ biomarker covered
50 testkits developed
5 diagnostics categories
1 Healthcare AI to explain epigenetic age

cerascreen
Genetic Age Test

The cerascreen® Genetic Age Test is a DNA test that allows you to calculate your actual biological age. The results report includes individualized recommendations based on a questionnaire to slow down cell aging and maintain your youth.

- + World first in DNA diagnostics
- + Experience biological age
- + Developed with Fraunhofer IME Institute
- + Recommendations to preserve youth

cerascreen test portfolio

agewatchers

Epigenetic Nutrients powered by cerascreen

The power of nature has been known for thousands of years. We have used high-tech methods to analyse the most valuable substances for a long life. The result is agewatchers - epigenetic nutrients.

+ Analysis of 630.000+ natural substances
+ Unique substance combinations
+ Developed with Fraunhofer IME Institute
+ Experience biological age

References

Jiang, R., Jones, M.J., Sava, F. et al. Short-term diesel exhaust inhalation in a controlled human crossover study is associated with changes in DNA methylation of circulating mononuclear cells in asthmatics. Part Fibre Toxicol 11, 71 (2014).

Sen, Payel et al. "Epigenetic Mechanisms of Longevity and Aging." Cell vol. 166,4 (2016): 822-839.

Szarc vel Szic, Katarzyna, et al. "From inflammaging to healthy aging by dietary lifestyle choices: is epigenetics the key to personalized nutrition?." Clinical epigenetics vol. 7,1 33. 25 Mar. 2015.

Oliveras-Ferraros, C., Fernández-Arroyo, S., Vazquez-Martin, A., Lozano-Sánchez, J., Cufí, S., Joven, J., Micol, V., Fernández-Gutiérrez, A., Segura-Carretero, A., Menendez, J. A."Crude phenolic extracts from extra virgin olive oil circumvent de novo breast cancer resistance to HER1/HER2-targeting drugs by inducing GADD45-sensed cellular stress, G2/M arrest and hyperacetylation of Histone H3". International Journal of Oncology 38.6 (2011): 1533-1547.

Caramia, G., Gori, A., Valli, E. and Cerretani, L. (2012), Virgin olive oil in preventive medicine: From legend to epigenetics. Eur. J. Lipid Sci. Technol., 114: 375-388. Edwin D. Lephart, John M. Sommerfeldt, Merritt B. Andrus, Resveratrol: influences on gene expression in human skin, Journal of Functional Foods, Volume 10, 2014, Pages 377-384, ISSN 1756-4646.

Maeda T, Oyama JI, Higuchi Y, Arima T, Mimori K, Makino N. The correlation between the telomeric parameters and the clinical laboratory data in the patients with brain infarct and metabolic disorders. J Nutr Health Aging. 2010;14(9):793-797.

Carmen P. Wong, Nicole A. Rinaldi, Emily Ho. Zinc deficiency enhanced inflammatory response by increasing immune cell activation and inducing IL6 promoter demethylation. Molecular Nutrition & Food Research, 2015.

Gu, Harvest & Zhang, Xiuli. (2017). Zinc Deficiency and Epigenetics. 10.1007/978-3-319-40007-5_80-1.

Boyanapalli, Sarandeep S S, and Ah-Ng. Tony Kong. "Curcumin, the King of Spices": Epigenetic Regulatory Mechanisms in the Prevention of Cancer, Neurological, and Inflammatory Diseases." Current pharmacology reports vol. 1,2 (2015): 129-139.

Azad GK and Tomar RS (2015) Epigenetics of Curcumin: A Gifted Dietary Therapeutics Compound. J Carcinog Mutagen 6: 206.

Raynal NJ, Lee JT, Wang Yet al (2016) Targeting calcium signaling induces epigenetic reactivation of tumor suppressor genes in cancer. Cancer Res 76:1494–1505

Dhawan D.K. Environment and Life Style Related Epigenetics: A clinical Preview. J. Clin. Epigenet. 2016;2:3.

Dolinoy D.C., Huang D., Jirtle R.L. Maternal nutrient supplementation counteracts bisphenol A-induced DNA hypomethylation in early development. Proc. Natl. Acad. Sci. USA. 2007;104:13056–13061.

Nicodemus-Johnson J., Sinnott R.A. Fruit and Juice Epigenetic Signatures Are Associated with Independent Immunoregulatory Pathways. Nutrients. 2017;9

Lukasz Huminiecki, Jarosław Horbańczuk, The functional genomic studies of resveratrol in respect to its anti-cancer effects, Biotechnology Advances, Volume 36, Issue 6, 2018, Pages 1699-1708.

Albanes D. Total calories, body weight, and tumor incidence in mice. Cancer Res 1987; 47(8): 1987-92.

Longo VD, Fontana L. Calorie restriction and cancer prevention: metabolic and molecular mechanisms. Trends Pharmacol Sci 2010; 31(2): 89-98.

Hernandez-Saavedra D, Moody L, Xu GB, Chen H, Pan YX. Epigenetic regulation of metabolism and inflammation by calorie restriction. Advances in nutrition (Bethesda, Md) 2019; 10(3): 520-36.

Lameira AG Jr, Françoso BG, Absy S, et al. Resveratrol reverts epigenetic and transcription changes caused by smoke inhalation on bone-related genes in rats. DNA Cell Biol 2018; 37(8): 670-9.

Schröter, David et al. "Amaranth's 2-Caffeoylisocitric Acid-An Anti-Inflammatory Caffeic Acid Derivative That Impairs NF-κB Signaling in LPS-Challenged RAW 264.7 Macrophages." Nutrients vol. 11,3 571. 7 Mar. 2019.

Tang, Y., Tsao, R., Mol. Nutr. Food Res. 2017, 61, 1600767.

Bag A, Bag N. Tea Polyphenols and Prevention of Epigenetic Aberrations in Cancer. J Nat Sci Biol Med. 2018;9(1):2-5.

Horvath, Steve. DNA methylation age of human tissues and cell types Genome Biology 14, no. 10 (2013): R115.

R. Obeid, U. Hübner, M. Bodis, S. Graeber, J. Geisel, Effect of adding B-vitamins to vitamin D and calcium supplementation on CpG methylation of epigenetic aging markers, Nutrition, Metabolism and Cardiovascular Diseases, Volume 28, Issue 4, 2018, Pages 411-417.

Fetahu, Irfete S et al. "Vitamin D and the epigenome." Frontiers in physiology vol. 5 164. 29 Apr. 2014.

Horvath, Steve, Chiara Pirazzini, Maria Giulia Bacalini, Davide Gentilini, Anna Maria Di Blasio, Massimo Delledonne, Daniela Mari, et al. Decreased epigenetic age of PBMCs from Italian semi-supercentenarians and their offspring Aging 7, no. 12 (December 2015): 1159–70.

Sae-Lee C, Corsi S, Barrow TM, et al. Dietary Intervention Modifies DNA Methylation Age Assessed by the Epigenetic Clock. Mol Nutr Food Res. 2018;62(23):e1800092.

Farias N., Ho N., Butler S., Delaney L., Morrison J., Shahrzad S., Coomber B.L. The effects of folic acid on global DNA methylation and colonosphere formation in colon cancer cell lines. J. Nutr. Biochem. 2015;26:818–826.

Davis Cd, Uthus Eo, Finley Jw. Dietary selenium and arsenic affect DNA methylation in vitro in Caco-2 cells and in vivo in rat liver and colon. J Nutr. 2000;130(12):2903–2909.

Xiang N, Zhao R, Song G, Zhong W. Selenite reactivates silenced genes by modifying DNA methylation and histones in prostate cancer cells. Carcinogenesis. 2008;29(11):2175–2181.

Lechner, John F, and Gary D Stoner. "Red Beetroot and Betalains as Cancer Chemopreventative Agents." Molecules (Basel, Switzerland) vol. 24,8 1602. 23 Apr. 2019.

Han, Ga Eun, et al. "Novel Neohesperidin Dihydrochalcone Analogue Inhibits Adipogenic Differentiation of Human Adipose-Derived Stem Cells through the Nrf2 Pathway." International journal of molecular sciences vol. 19,8 2215. 29 Jul. 2018.

Choi JM, Yoon BS, Lee SK, Hwang JK, Ryang R. Antioxidant properties of neohesperidin dihydrochalcone: inhibition of hypochlorous acid-induced DNA strand breakage, protein degradation, and cell death. Biol Pharm Bull. 2007;30(2):324-330.

Szyf M, Mcgowan P, Meaney Mj. The social environment and the epigenome. Environ Mol Mutagen. 2008;49(1):46–60.

Jirtle Rl, Skinner Mk. Environmental epigenomics and disease susceptibility. Nat Rev Genet. 2007;8(4):253–262.

Murgatroyd C, Patchev Av, Wu Y, et al. Dynamic DNA methylation programs persistent adverse effects of early-life stress. Nat Neurosci. 2009;12(12):1559–1566.

Hirayama J, Sahar S, Grimaldi B, Tamaru T, Takamatsu K, Nakahata Y, Sasson Corsi P. CLOCK-mediated acetylation of BMAL1 controls circadian function. Nature. 2007;450 (7172):1086–1090.

Costa G. The problem: shiftwork. Chronobiol Int. 1997;14(2):89–98.

Bollati V, Baccarelli A, Sartori S, et al. Epigenetic effects of shiftwork on blood DNA methylation. Chronobiol Int. 2010;27(5):1093–1104.

Sharma, Manvi et al. "The Epigenetic Connection Between the Gut Microbiome in Obesity and Diabetes." Frontiers in genetics vol. 10 1329. 15 Jan. 2020.