WHAT THE REPORT INCLUDES

- Detailed EXPLANATION of the test performed and recommendations to be followed;
- SUMMARY TABLE showing the metabolic areas investigated and the results obtained the DNA analysis, in order to have a quick overview of one's general situation and to check for compromised situations;
- BIBLIOGRAPHY providing scientific references for the test.

COLOURS USED

Green indicates that the variants identified in the analysis do not unfavourably alter enzymatic activity of the proteins they encode and/or the risk associated with certain diseases.

Orange indicates that the variants identified in the analysis slightly unfavourably alter enzyme activity and/or the risk associated with certain disorders or diseases.

Red indicates that the variants identified in the analysis alter enzyme activity in a particularly unfavourable way, resulting in an increased risk of developing certain disorders or associated diseases.

The results shown, as well as the considerations and explanations contained in the following pages of this booklet, should not be regarded as a medical diagnosis. It is important to bear in mind that the genetic information is only a part of the total information needed to gain a complete picture of a person's state of health, and the data reported here is therefore a tool available to the treating physician to formulate a correct assessment of the patient's physiological state and suggest an appropriate personalised treatment.

INTRODUCTION

Longevity, understood not only as the length of life but above all as the quality of the years lived, is the result of a complex interweaving of genetic, environmental, and behavioural factors. In addition to genetic inheritance, daily interactions with the environment, diet, lifestyle, and exposure to various stressors contribute greatly to the ageing process.

From conception, our organism possesses biological foundations that can be affected, both positively and negatively, by a series of biochemical phenomena such as oxidative, inflammatory and glycation processes. Over the years, the accumulation of cellular damage, altered immune response and epigenetic changes (such as DNA methylation) contribute to a progressive decline in the body's capacity for regeneration and resistance.

The longevity test we propose is based on the analysis of specific biomarkers of ageing, including:

1. Inflammaging: the presence of a chronic low-grade inflammatory state that may favour the development of degenerative diseases.
2. Glycation: the accumulation of advanced glycation end-products, which impair protein function and accelerate tissue deterioration.
3. Methylation: epigenetic changes that regulate gene expression and can influence the ageing process.
4. Oxidative stress: the damage induced by free radicals, the balance of which with antioxidant mechanisms is essential for maintaining cell function.

Through an integrated analysis of these indicators, the test does not aim to provide a biological age, but to paint a detailed picture of the organism. In this way, any imbalances can be detected early and personalised interventions can be prepared that can slow down the natural ageing process, improve health management and prevent related diseases.

1. INFLAMMAGING

It is well known that ageing brings with it a state of chronic inflammation. In practice, with age our organism manifests an increased presence of inflammation, which can activate tissue damage and contribute to the development of various age-related diseases.

This phenomenon has been termed inflammaging (inflammation associated with ageing) and represents the systemic inflammatory state observed in many pathological conditions in the elderly.

A key role in this process is played by **interleukin-6 (IL6),** a key cytokine for the immune response. IL6 coordinates the inflammatory response, helping the body to react against infections and injuries. However, certain genetic variants of IL6 can affect levels of chronic inflammation, increasing the risk of cardiovascular, neurodegenerative, and other age-related diseases.

Immunological studies focus on IL6 to better understand how this protein interacts with the immune system and contributes to both protection and the development of inflammatory diseases. Fully understanding the role of IL6 could pave the way for new preventive and therapeutic strategies to improve health during ageing.

YOUR RESULT:

ID Gentras	Gene	Allelic variants	Genotype		Predisposition
INFLAMMAGING					
GTS006	IL6	G	C	C	HIGH
(Interleukin 6)		C			

WHAT YOUR GENETICS SAY

In the presence of an unfavourable genetic profile for the analysed gene.

EFFECTS OF THE UNFAVOURABLE VARIANT:

The unfavourable variant related to the interleukin-6 (IL6) gene can lead to increased production or altered regulation of this cytokine, resulting in an increased chronic inflammatory response. In practice, those with this variant tend to maintain high levels of inflammation over time, even in the absence of infection or acute injury. This results in:

- increased systemic inflammation
- predisposition to autoimmune diseases
- risk of obesity and insulin resistance
- neuro-inflammation

RECOMMENDED SOLUTIONS :

To mitigate the effects of this unfavourable variant and manage the inflammatory state, several solutions are recommended:

- Recovery of a correct dietary approach, very close in aspects and content to the classic Mediterranean diet.
- Regular, well-balanced, and motor activity with a structured programme.
- Specific and targeted oral additions:
    - *Omega 3*: eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA): these are the main constituents of a category of supplements known as fish oil, and algae oil (if EPA-free).
    - *Boswellia serrata*: the anti-inflammatory effect is related to its ability to inhibit certain reactions, just like the more classic anti-inflammatory agents.
    - *Curcuma longa*: has an anti-inflammatory effect in both the acute and chronic phases. It is best combined with black pepper, which increases its bioavailability.
    - *Resveratrol*: a natural polyphenol capable of exerting both antioxidant and anti-inflammatory activity.

Adopting an integrated approach combining these interventions may help to offset the effects of the unfavourable variant, improving the management of the inflammatory state and, consequently, quality of life and long-term health.

2. GLYCATION

Glycation is a process that occurs when sugar in the blood incorrectly attaches to proteins, creating abnormal bonds (cross-linking) between them. When glucose levels are irregular or insulin is not produced and utilised correctly, this process occurs more easily. The result is protein damage that can impair:

- The expression of genes (i.e., the way genetic information is read and used by cells);
- The synthesis of new proteins.
- The proper functioning of the immune system.

In summary, glycation damages cells and tissues, contributing to the deterioration associated with ageing. For this reason, it is considered one of the main biomarkers (indicators) of the ageing process.

A further element to consider concerns the **Peroxisome proliferator-activated receptor gamma (PPARG)** gene, which regulates fat metabolism and insulin sensitivity. There are several variants of this gene:

- Pro/Pro (unfavourable) variant: It is linked to increased insulin resistance, which means that the body struggles to utilise sugar efficiently. This can lead to obesity and an increased risk of developing type 2 diabetes.
- Pro/Ala variant: Has an intermediate effect, with partial risks and benefits.
- Ala/Ala variant (favourable): It is associated with improved insulin sensitivity, reducing the risk of metabolic problems.

Thus, when blood sugar levels are not well controlled, glycation can damage proteins and, consequently, contribute to ageing. Furthermore, the variant present in the PPARG gene can influence how efficiently the body handles glucose and fat, leading to a higher or lower risk of metabolic problems and premature ageing.

YOUR RESULT:

ID Gentras	Gene	Allelic variants	Genotype		Predisposition
GLICATION					
GTS006	**PPARG**	**G**	**C**	**C**	**HIGH**
(peroxisome proliferator activated receptor-2)		**C**			

WHAT YOUR GENETICS SAY

In the presence of an unfavourable genetic profile for the gene analysed.

EFFECTS OF THE UNFAVOURABLE VARIANT

The unfavourable variant, in this case the Pro/Pro variant of the PPARG gene, leads to less sensitivity to insulin. In other words, the body's cells respond less effectively to insulin, making it more difficult to utilise blood sugar. This can result in:

- Increased insulin resistance, and thus increased susceptibility to type 2 diabetes.
- Increased accumulation of visceral fat, and thus increased risk of obesity.
- Altered lipid metabolism: increased triglycerides and LDL, with higher cardiovascular risk.

RECOMMENDED SOLUTIONS

To try to counteract these effects, here are some recommended solutions:

- Balanced, low glycaemic index diet:
  - Prefer whole foods, fruit, vegetables, pulses and whole grains that help keep blood sugar levels stable.
  - Limit refined sugars and simple carbohydrates, which can cause glycaemic spikes.
- Regular physical activity:

  - Exercise, both aerobic and endurance, helps improve insulin sensitivity and control body weight.

  - Even a simple daily walk can make a difference.
- Stress management:

  - Chronic stress can worsen insulin resistance. Relaxation techniques, meditation or yoga can help reduce it and improve general well-being.

- Medical monitoring:

  - Regularly monitoring glucose levels and other metabolic parameters allows early intervention if alterations are noticed.

  - The doctor's support can guide any specific therapeutic or nutritional choices, e.g. the use of useful supplements such as carnosine, vitamin B6 (pyridoxamine), zingibar officinalis and alpha-lipoic acid. Recent scientific literature has highlighted the anti-platelet potential of a herb, Aerva lanata.

3. METHYLATION

Methylation is a process that helps form and repair DNA, control cell growth and regulate which genes are switched on or off. If this process does not work properly, the body ages more rapidly.

An important gene in this pathway is **Methylenetetrahydrofolate reductase (MTHFR)**, which helps manage homocysteine and folic acid in the body. Different variants of this gene influence the efficiency of the enzyme:

- T/T variant (unfavourable): The enzyme works less well, causing high homocysteine levels, which can increase the risk of heart problems.

- C/T variant: The enzyme functions at an intermediate level.
- C/C variant (favourable): the enzyme functions normally, maintaining the balance of homocysteine levels.

YOUR RESULT:

ID Gentras	Gene	Allelic variants	Genotype		Predisposition
METHYLATION					
GTS006	**MTHFR**	**C**	**T**	**T**	**HIGH**
(methylene tetrahydrofolate reductase)		**T**			

WHAT YOUR GENETICS SAY

In the presence of an unfavourable genetic profile for the gene analysed.

EFFECTS OF UNFAVOURABLE VARIANTS

The unfavourable variant of the MTHFR gene can have several negative effects on our organism:

- Increased homocysteine levels: excessively high levels of this amino acid in the blood are linked to an increased risk of heart problems.
- Altered folate metabolism: poor folate metabolism may adversely affect fertility.
- Neurological problems: reduced production of neurotransmitters may make people more susceptible to anxiety, depression, and cognitive problems (such as memory or concentration difficulties).

RECOMMENDED SOLUTIONS

To counteract these effects, some practical solutions are recommended:

- Use of active folates:
  - It is preferable to take active folates (such as 5-MTHF or methylfolate) instead of conventional folic acid because the body utilises them better.
- Balanced diet:
  - Follow a diet rich in green leafy vegetables, legumes, citrus fruits and lean proteins. These foods are good sources of folate and other essential nutrients.
- Supplementation with vitamins and betaine:
  - Vitamin B1: Important for metabolism and found in foods of animal origin.
  - Vitamin B6: Aids nutrient metabolism and is found in eggs, chicken, fish, liver, nuts, beer and legumes (especially soya) and whole grains.
  - Betaine: A powerful methylating agent that supports the methylation process and helps reduce homocysteine levels.

These measures can help improve folate metabolism, keep homocysteine levels under control and, in general, reduce the health risks associated with the unfavourable variant of the MTHFR gene.

4. Oxidative stress

Oxidative stress occurs when there are too many reactive chemical compounds in the body, such as certain oxygen and nitrogen species and free carbon radicals. These compounds, in excess, can damage cells.

The causes of this increase may be external, such as:

- Ultraviolet radiation
- Chemical substances (hydrocarbons, herbicides, food contaminants, drugs)
- Infections (viruses and bacteria)

Internal causes may also contribute, for example:

- Genetic mutations that reduce the efficiency of antioxidant enzymes produced by the body.
- An accelerated cell metabolism.
- Diseases such as obesity and diabetes

When the body fails to maintain the balance between the production and removal of free radicals, cell damage occurs which, if prolonged, can accelerate ageing and promote the development of various diseases.

The **Super Oxide Dismutase Type 2 (**SOD2) gene produces an enzyme that is essential for eliminating free radicals. This enzyme works best when it is located in the mitochondrion, the 'energy centre' of the cell. If the SOD2 enzyme is not in the right place, its activity is reduced, leaving cells more exposed to free radical damage. In fact, cells use these enzymes to protect themselves from damage caused by external factors (such as radiation and pollution) and free radicals produced during normal

functioning. In essence, without SOD2, cells would not be able to defend themselves, compromising the health of the entire body.

By analysing a specific variant of the SOD2 gene, we can understand whether the enzyme is present in the right place and whether it is functioning correctly. People with a less active version of SOD2 are at greater risk of free radical damage.

YOUR RESULT:

ID Gentras	Gene	Allelic variants	Genotype		Predisposition
OXIDATIVE STRESS					
GTS006	**SOD2**	**T**	**C**	**C**	**HIGH**
(Superoxide Dismutase Type 2)		**C**			

WHAT YOUR GENETICS SAY

In the presence of an unfavourable genetic profile for the gene analysed.

EFFECTS OF THE UNFAVOURABLE VARIANT:

The unfavourable variant can lead to several negative effects:

- High oxidative stress: This means that the body produces too many free radicals, substances that damage cells and can make the body age faster.
- Increased risk of neurodegenerative diseases: Brain cells can be damaged, increasing the risk of diseases such as Alzheimer's or Parkinson's.
- Predisposition to heart problems and hypertension: The damage caused by free radicals can contribute to heart problems and increased blood pressure.
- Problems in the mitochondria: These 'energy centres' of cells can be damaged, which has a negative impact on metabolism (energy production) and inflammation.

RECOMMENDED SOLUTIONS:

To counteract these effects, several solutions are recommended:

- Daily intake of antioxidants:
  - Nutraceuticals such as alpha-tocopherol (a form of vitamin E) and lipoic acid help 'clean up' free radicals in the body.
  - Resveratrol, quercetin, and hesperidin, which have antioxidant properties, can also be supplemented.
- Diet rich in antioxidant foods:

Consuming lots of fruit and vegetables helps provide vitamins and substances that fight free radicals, especially vitamins A, C, E and beta-carotene.
Some recommended foods are:

- Blueberries and red fruits: Rich in vitamin A, C and anthocyanins.
- Carrots: Source of beta-carotene and vitamin C.
- Kiwi and citrus fruits: Excellent sources of vitamin C.
- Beets: Contain vitamin B9, C and potassium.
- Goji berries: Considered to be true antioxidant superfoods.
- Dark chocolate: Rich in flavonoids.
- Green and white tea: Full of polyphenols and catechins.
- Oil seeds and nuts: Excellent sources of healthy fats and antioxidants.

These measures help protect cells from oxidative stress, reducing the risk of premature ageing and cell damage-related diseases.