SKIN CARE

INTRODUCTION

Our skin, especially the face, is the mirror of our age, and the first signs of aging are visible already after the age of 30. Time cannot be stopped, but many of the consequences it has on the skin can certainly be slowed down. The most effective way is prevention.

Skin aging depends on chrono-aging, a natural process linked to the passage of time and based on one's genetics, and on photo-aging, i.e., the action of sun rays on the skin and lifestyle factors such as diet, physical activity, smoking, drugs, etc.

However, the negative action of time on the skin is not the same for all individuals but depends on predisposing factors written in our DNA. The presence of variants (SNPs) in the genes involved in these physiological processes can, in fact, modulate individual susceptibility, determining a different response to environmental agents and, consequently, influencing the skin aging process. The concept of personalized prevention is based on this assumption: if we know the characteristics of our body through the study of DNA, we can act in the most effective way to make it function optimally.

The genetic test allows us to highlight the main areas of weakness in the fundamental components of the skin structure.

WHAT THE REPORT INCLUDES:

- Detailed Explanation of the specific test conducted and recommendations to follow.
- Summary Table showing the list of metabolic areas investigated for each test and the summary of the respective results obtained from the analysis of your DNA, providing a quick overview of your general situation and highlighting any compromised areas.
- Bibliography containing the scientific references of the test.

HOW TO INTREPRET THE RESULTS:

Low Risk: Indicates that the variants identified in the analysis do not unfavorably alter the enzymatic activity of the proteins they encode and/or do not increase the risk associated with certain pathologies.

Moderate Risk: Indicates that the variants identified in the analysis slightly unfavorably alter the enzymatic activity and/or slightly increase the risk associated with some disorders or pathologies.

High Risk: Indicates that the variants identified in the analysis significantly unfavorably alter the enzymatic activity, resulting in a higher risk of developing certain associated disorders or pathologies.

The illustrated results, along with the considerations and explanations contained in the following pages of this booklet, should not be considered a medical diagnosis. It is important to remember that genetic information is only part of the total information necessary for a complete understanding of a person's health. Therefore, the data reported here serve as a tool for the treating doctor to make a correct evaluation of the patient's physiological state and suggest an appropriate personalized treatment.

SKIN AGING EVOLUTION

1. PHOTOAGING

The test evaluates the risk of skin aging with respect to extrinsic factors, namely:

SUSCEPTIBILITY TO ULTRAVIOLET RAYS: UVA AND UVB

Sensitivity to the harmful effects of ultraviolet radiation is heritable. Numerous large-scale studies have identified genetic variations that increase sensitivity to the sun and the tendency to suffer from sunburn (erythema). Some people's skin is therefore 3-4 times more vulnerable to sun damage. In these cases, there is a tendency to develop freckles, a greater propensity not to tan easily, and to suffer sunburn.

RECOMMENDED SOLUTIONS:

- Use high protection creams (preferably with added vitamin A).
- Expose yourself to the sun for a limited time every day and prefer the sun in the first part of the morning or the second part of the afternoon.
- Protect the area around the eyes very well, using sunglasses.

Failure to follow these precautions with great discipline will almost inevitably lead to rapid skin aging, in the form of loss of skin elasticity, and the appearance of premature blemishes and wrinkles.
The genetic analysis examines the following gene:

- Gene responsible for the risk of extrinsic skin aging: ASIP (Agouti Signaling Protein)

Repeated exposure to ultraviolet radiation (UVA, UVB) causes premature skin aging. The effect is achieved through DNA damage to epidermal cells, persistent inflammation, and oxidative stress. The analysis of two variants of a point in this gene reveals whether the individual examined falls into the category of those who have skin that is more sensitive than the general population to environmental insults, primarily solar radiation and UV emissions from tanning lamps, and therefore a greater tendency to skin aging. In the European population, 55% of individuals fall into this category.

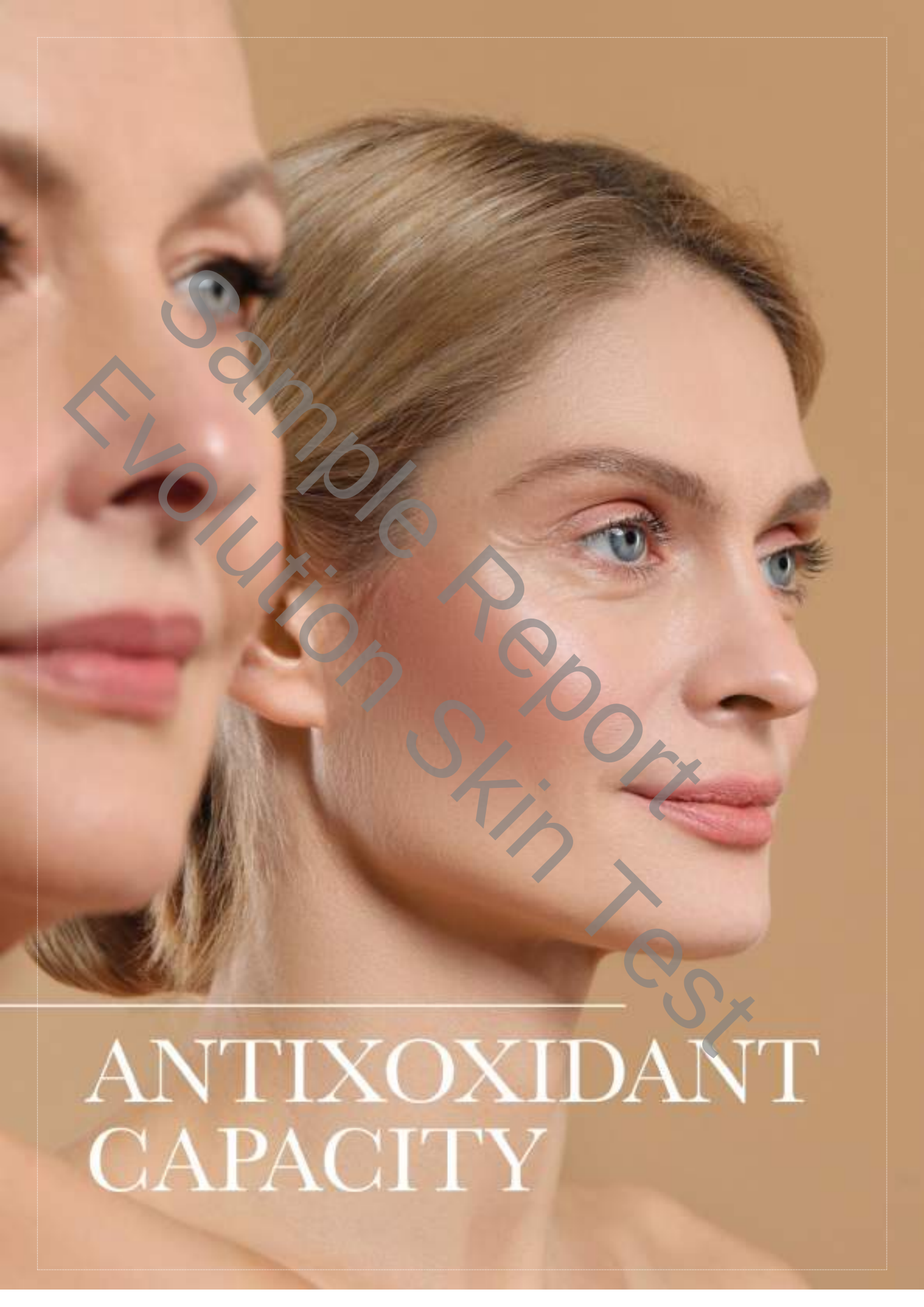
The information acquired allows us to formulate a correct strategy to protect the skin from premature aging.

YOUR RESULTS:

Lab ID	Gene	Allelic variants	Genotype		Predisposition
EXTRINSIC SKIN AGING					
GTS005	**ASIP**	**G**	**G**	**G**	**LOW**
(Agouti Signaling Protein)		**T**			

WHAT YOUR GENETICS SAY

There is a FAVORABLE genetic profile for the analyzed gene



ANTIXOXIDANT CAPACITY

2. ANTIOXIDANT CAPACITY

The test evaluates the risk of skin aging with respect to intrinsic factors, namely:

SUSCEPTIBILITY TO DAMAGE CAUSED BY FREE RADICALS

An essential enzyme for the removal of free radicals (SOD2), which is less functional (with half the efficiency) when not localized in its natural site of action, the mitochondrion, exposes a person to the possibility of greater damage from free radicals produced physiologically by all the cells of their organism. This will have a "visible" effect, especially at the epidermis level, with a greater tendency towards skin aging, presenting as thin, atrophic, pale, loose skin, extensively furrowed by wrinkles and inelastic.

RECOMMENDED SOLUTIONS:

- Daily and continuous oral intake of strong antioxidant nutraceuticals. Alpha-tocopherol and lipoic acid are recommended, as they have a well-documented effect as scavengers of oxygen radicals produced at the respiratory chain level.
- A healthy and balanced diet includes the intake of many foods' rich in antioxidants such as fruits and vegetables. In particular, the intake of vitamins A, C, and E, and beta-carotene is essential. The best foods against free radicals are:
  - Blueberries and red fruits, rich vitamin A, vitamin C and anthocyanin glycosides
  - Carrots, rich in beta carotene and vitamin C
  - Kiwis and citrus fruits rich in vitamin C
  - Beets rich in vitamin B9, vitamin C, and potassium
  - Goji berries, real antioxidant superfoods
  - Dark chocolate rich in flavonoids
  - Green tea and white tea, rich in polyphenols and catechins
  - Oilseeds and nuts

The genetic analysis examines the following gene:
• Gene responsible for intrinsic skin aging risk: SOD2 (SuperOxide Dismutase type 2)

The antioxidant activity of the cells of the epidermis is the main way in which they defend themselves from the damage of ultraviolet radiation, other environmental factors such as air pollutants and smoke, and from free radicals that are normally produced within the cells themselves. Antioxidant activity depends on various genes, among which the one for the SOD2 protein stands out, which is found in the mitochondria, the energy centers of the cells where most intrinsic free radicals are produced. SOD2 is so important that life is not possible in its absence. The analysis of the variant of a point of this gene allows us to understand whether it will have its correct localization and action in the mitochondria. Consequently, it indicates its greater or lesser activity. Those with lower SOD2 activity than the general population will consequently be more exposed to damage from free radicals.
The information acquired allows us to formulate a correct strategy to support the antioxidant activity of epithelial cells with targeted food supplements and cosmeceutical creams.

YOUR RESULTS:

Gentras ID	Gene	Allelic variants	Genotype		Predisposition
INTRINSIC AGING					
GTS006	**SOD2**	**T**	**C**	**C**	**HIGH**
(SuperOxide Dismutase type 2)		**C**			

WHAT YOUR GENETICS SAY

There is an UNFAVORABLE genetic profile for the analyzed gene, we recommend the use of antioxidant nutraceuticals (please see above).

ACNE

3. ACNE

Acne is the most common skin disease, very widespread among adolescents and young people (affecting more than 85% of adolescents), although it can also occur in adults. It affects the sebaceous glands, which are connected to the pores of the skin through a channel called a follicle. These glands produce a fatty substance called sebum, which carries dead cells to the surface of the skin through the follicle. When a follicle is blocked, a pimple occurs, and bacteria within the follicle cause swelling.

RECOMMENDED SOLUTIONS:

Use of anti-acne drugs (even with antibiotic action) to be applied directly to the skin and also pills.
In addition to hormonal changes, stress, some medications, and the use of makeup that blocks the follicles, there are hereditary factors that contribute more than 78% to the appearance of acne, especially the gene:

- FST (Follistatin) rs629725 A allele

The FST gene encodes a soluble protein, follistatin, which binds and neutralizes members of the TGF-β superfamily of cytokines, called transforming growth factors-beta (TGF-β). The function of this family of cytokines is to transmit inflammatory signals from the cell surface to the cell through a process of signal transduction. If there is no balance of these factors, hyperactivity of the sebaceous glands, inflammation of the follicles, and outsized growth of the Propionibacterium acnes bacterium occur. When overexpressed, follistatin causes very slow healing of acne and, by binding to activin, causes thinner and fibrotic skin to develop.

YOUR RESULTS:

Gentras ID	Gene	Allelic variants	Genotype		Predisposition
PREDISPOSITION TO ACNE					
GTS0XX	**TGFB2**	**T**	**T**	**T**	**LOW**
(Transforming growth factor-beta 2)		**A**			

WHAT YOUR GENETICS SAY

There is a FAVORABLE genetic profile for the analyzed gene

SKIN INFLAMMATION

4. SKIN INFLAMMATION

Skin inflammation occurs when skin cells have a hyper-reactive response to allergens or toxins. Acute inflammation is a natural reaction that aims to repair the skin after exposure to infections or environmental toxins and usually lasts a few days. While this is a useful short-term response, prolonged inflammation can have detrimental effects. Chronic inflammation becomes destructive and damages the skin. There are numerous factors that can induce chronic inflammation: UV rays, stress, toxins, tobacco, alcohol, infections from pathogens, and excess free radicals. Although inflammation is the skin's first line of defense, an excessive inflammatory response can prematurely age the skin. Signs of chronic inflammation include skin tenderness, redness, and irritation.

RECOMMENDED SOLUTIONS:

- Daily and continuous intake of potent antioxidant nutraceuticals is recommended. Coenzyme Q10 and Vitamin E, in particular, are beneficial.

Genetic variations in various pro-inflammatory and anti-inflammatory genes are associated with an increased risk of chronic skin inflammation, particularly in genes like:

- Gene: IL-18 (Interleukin-18) (rs187238-137 G/C)

Interleukin-18 is a potent pro-inflammatory cytokine (member of the IL-1 family) with numerous biological activities that stimulate both inflammation and the immune system. It is produced by normal skin constituents, including keratinocytes, fibroblasts, and dermal endothelial cells, as well as by inflammatory cells that infiltrate the skin during various pathological conditions. In fibroblasts, its overexpression inhibits collagen production and promotes the formation of skin scars.

YOUR RESULTS:

Gentras ID	Gene	Allelic variants	Genotype		Predisposition
SKIN INFLAMMATION					
GTS0XX	**IL-18**	**G**	**G**	**C**	**INTERMEDIATE**
(Interleuchina-18)		**C**			

WHAT YOUR GENETICS SAY

There is an INTERMEDIATE genetic profile (with only one UNFAVORABLE variant) affecting the analyzed gene, which however predisposes to skin inflammation.

VARICOSE VEINS

5. VARICOSE VEINS

Varicose veins are small veins that appear as strong purple-blue protrusions under the skin. They affect more than a third of the world's population and can cause pain, itching, ulceration, and venous thrombosis. There are simple measures to prevent varicose veins.

RECOMMENDED SOLUTIONS:

- Engage in regular physical exercise.
- Maintain a healthy diet.
- Avoid prolonged periods of standing or sitting.
- Elevate your legs.
- Avoid wearing high-heeled shoes and crossing your legs.

Non-genetic risk factors include obesity, age, prolonged sitting or standing, and hormonal changes. Those with a family history of varicose veins are more susceptible, and genetic variations in the MTHFR gene increase the risk.

The specific countermeasure against this unfavorable variant is:

- Daily oral intake of folic acid
- Daily oral intake of Vitamin E to strengthen vein endothelium walls.

We examine two mutations in the MTHFR (Methylene tetrahydrofolate reductase) gene.

MTHFR is an enzyme that affects the efficiency of folic acid metabolism. Folic acid, a water-soluble vitamin of the B group (Vitamin B9), is essential for crucial cellular processes: biosynthesis of purine nucleotides, which are precursors of nucleic acids; methylation reactions; homocysteine metabolism; and other important biochemical reactions, particularly during periods of rapid cell division and growth. Because of this, both children and adults require folic acid for optimal health. Folic acid intake also influences skin health; it is known to participate in repairing DNA damage caused by solar radiation and in improving the biomechanical characteristics of the skin.

The second SNP (GTS016) has also been correlated with various skin disorders. Folate, the inactive form of the vitamin found in foods, is converted into its active form in the intestine through two reduction reactions. The second reaction is catalyzed by the MTHFR enzyme, leading to the production of tetrahydro folic acid.

YOUR RESULTS:

Lab ID	Gene	Allelic variants	Genotype		Predisposition
VARICOSE VEINS					
GTS003	**MTHFR** (metilen tetraidrofolato reduttasi)	**C** **T**	**T**	**T**	**HIGH**

Lab ID	Gene	Allelic variants	Genotype		Predisposition
VARICOSE VEINS					
GTS016	**MTHFR-2** (metilen tetraidrofolato reduttasi)	**A** **C**	**A**	**C**	**INTERMEDIATE**

WHAT YOUR GENETICS SAY	
	
MTHFR *A HIGH SUSCEPTIBILITY genetic profile is present indicating reduced folate metabolism.*	**MTHFR-2** An INTERMEDIATE SUSCEPTIBILITY genetic profile is present indicating likelihood of skin disorders.

CELLULITE

6. CELLULITE

Cellulite is a common aesthetic concern affecting many women (80-90%), characterized by alterations to the skin surface that give it an uneven and unsightly appearance. This condition results from irregular fibrous tissue and the accumulation of subcutaneous fat. It predominantly affects the buttocks, hips, and thighs, though it can also occur on other body parts such as the abdomen.

Many people believe that cellulite only affects overweight women; however, approximately 80% of women will develop some form of cellulite regardless of their weight.

Caucasian women are more susceptible to cellulite compared to Asian women, partly due to dietary differences. The causes of cellulite are multifaceted and involve hormonal factors, the circulatory system, the extracellular matrix, inflammation, substances produced by adipocytes, genetic predisposition, and fluctuations in weight.

RECOMMENDED SOLUTIONS:

- Maintain a healthy weight
- Stay active
- Stay hydrated
- Use anti-cellulite creams
- Receive massages and consider medical-aesthetic treatments beneficial in treating this disorder.

Variations in the HIF1A (Hypoxia-inducible factor-1α) gene (rs11549465 1772C/T) have been associated with an increased risk of developing cellulite. HIF1A, along with other genes in the HIF family, belongs to a superfamily of transcription factors. This gene is activated under conditions of low oxygen availability (hypoxia) and regulates various downstream genes in response to hypoxic stress. In the case of this missense mutation, which alters an amino acid in the protein, over-expression occurs in the keratinocytes of the skin. This leads to hypoxia in adipose tissue, dysregulation of lipid metabolism, and inflammation in adipose tissue.

Lab ID	Gene	Allelic variants	Genotype		Predisposition
CELLULITE					
GTS00X	**HIF1A**	**C**	**T**	**T**	**HIGH**
(Hypoxia Inducible Factor 1 Subunit Alpha)		**T**			

WHAT YOUR GENETICS SAY

There is a genetic profile with HIGH PREDISPOSITION to the development of cellulite (both variants UNFAVORABLE) affecting the gene analyzed.