



# TrichoTest™

## Results report



Genomics

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### **PERSONAL DATA**

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**Patient Code**     TRI14784AA

**Doctor's name**     Doctor Demo Fagron NL

**Report date**        03-02-2022



# WHAT CAN WE FIND OUT ABOUT YOU IN THIS GENETIC REPORT?

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## 01 WHY ARE GENETICS SO IMPORTANT TO ME?

The study of our genes enables us to understand the genetic load inherited from our parents. Having this information enables us to understand:

- Why we are unique
- How our bodies function
- Our individual susceptibility to hair loss.

All human beings are composed of cells. Each cell contains a copy of our genes and defines us as human beings. Each gene gives a specific instruction to our body, telling it how to function.

This is why genetics is a basic pillar of medicine and health in today's world. However, not everything is good for everybody. With genetics we can enter into a new era of preventative and personalized medicine by being much more precise and effective when approaching treatment for hair loss.



## 02 MOST RELEVANT TYPES OF ALOPECIA

Hair loss (alopecia) has different causes. These causes range from greater hereditary sensitivity in hair follicles to masculine sex hormones, infections, stress, disorders of the immune system, iron deficiency and medical treatments like chemotherapy.

### **Androgenic alopecia (hereditary alopecia)**

The term androgenetic alopecia is used when the cause of hair loss is hereditary, that is, it has a genetic basis. For this reason it is also called hereditary alopecia or genetically determined alopecia. In this case there is hypersensitivity of hair follicles to masculine hormones also referred to as androgens.

Although there are various causes of alopecia, there is no clear answer as to why there are different areas of baldness on the scalp. Alopecia often originates inside the hair follicle. These “production plants” are located below the skin and they are very susceptible to certain external factors. The vulnerable hair follicles will for instance have a large number of connection areas or receptors for Testosterone and Dihydrotestosterone hormones.

Dihydrotestosterone or DHT is a derivative of Testosterone created by the enzyme 5-alpha-reductase. DHT interacts with genetically affected receptors in hair follicles, shortening their growth phase and thus accelerating the hair growth cycle. As a result, the hair loses thickness and finally the hair follicle degenerates. Experts call this process miniaturisation of the follicle.

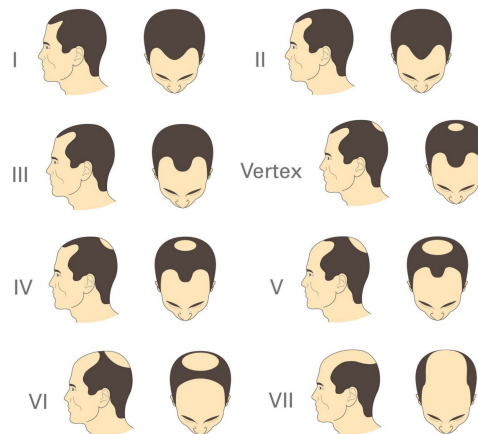
### Genetics

The development of androgenic alopecia is determined by hereditary factors (genes). This is why we use the term 'hereditary' alopecia as several genes play a vital role. Androgenic alopecia is caused by polygenic or multifactorial hereditary transmission. This explains, for example, why the abundance of hair of the grandfather (on the mother's or father's side) can be quite different from that of the father or the son. That is, there is no direct relationship between the type of hair of one direct family member and another because not only must they be genetically susceptible to the complaint, but other external factors must also favour its appearance.

According to scientific studies the tendency to hereditary hair loss is mainly transmitted through the mother via the androgen receptor. In this area the hair follicle binds to masculine sex hormones and transmission occurs through the X chromosome. As men can only inherit the X chromosome from their mother the 'risk' of suffering alopecia is more closely related to the mother or maternal grandfather rather than the father. However, hereditary factors are not the only causes of baldness. Other genes are involved irrespective of the paternal type, and so, on occasions, the susceptibility to alopecia may also be transmitted directly from father to son.

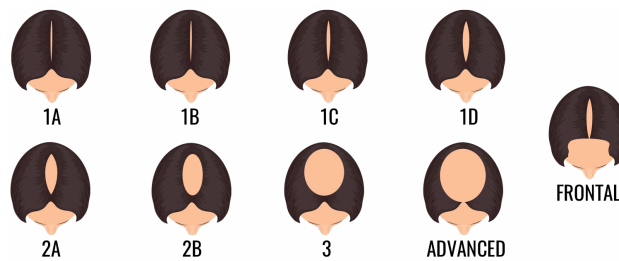
There are many factors that determine the appearance of androgenic alopecia in men and women. The degree of influence is highly variable. Some elderly men only have a slight receding hairline whereas others are completely bald at a very early age. The appearance of hereditary alopecia may also vary within the same family. The son or daughter of a bald father or a mother with hair loss may have abundant hair. On the other hand, a man or woman with a lot of hair may have children who will later suffer from hair loss.

Androgenic alopecia classification scales depending on the degree of baldness:



Hamilton-Norwood Scale (for men):

- **TYPE I-II:** There is a slight recession of the hairline around the temples.
- **Type III-IV:** Receding hairline and thinning hair on the vertex.
- **Type V:** Patterns at both sites are bigger but a thin division line is still present.
- **Type VI-VII:** The most severe form of hair loss. Little hair on the front or top of the head.



Ludwing Scale (for women):

- **Type 1:** Miniaturization of follicles results in thinning of the hair on the front and on top of the scalp.
- **Type 2:** Extended thinning on the front and top of the scalp, while hairline is preserved.
- **Type 3:** Balding only on the front and upper area of the scalp. Hairline is preserved.

## Alopecia areata

Alopecia occurs in round patches typically with no warning, without outside causes and has a circular or oval appearance. According to the current state of knowledge it is the result of an autoimmune disease. Alopecia areata may appear at any age, usually occurs within the same family and more commonly appears before 30 years of age.

The exact cause of alopecia areata is not known. Possible relationships such as hormonal disorders, intoxication with poisons or similar dangerous substances are being considered. Spot baldness or alopecia in round patches is not usually related to psychological causes.

## Telogen effluvium

Hair loss caused by haemoglobin deficiency or inadequate nutrition, drugs, hormones, stress, contaminants, etc. Telogen Effluvium occurs uniformly all over the scalp and can be differentiated from androgenic alopecia or alopecia areata by this unique characteristic.

### IMPORTANT NOTE:

This test is not, nor does it presume to be, a clinical diagnosis. It should always be interpreted with the aid of a trustworthy healthcare professional. This will ensure you gain maximum benefit from the results of this DNA test to aid treatment of your alopecia.

## 03 WHAT PROCEDURE IS USED FOR A GENETIC ANALYSIS?

### Genetic bioengineering

It all begins with a small sample of saliva. One of our molecular biology laboratory technicians then uses a series of biological reactions to extract the DNA from the cells present in the saliva.

Once extracted another series of laboratory processes purifies it, separating the DNA from the other parts of the cells. Once we have pure DNA we begin the amplification phase which consists of making copies of the DNA (this enables us to have more DNA to make the analysis without having to get more from the patient).

After all this has been completed the amplified DNA is analysed using our exclusive microarrays, small DNA chips that enable identifying the genes in the sample. In this case the chip is designed to identify genes containing information about alopecia.



## Technical information about the technology used in our laboratory

Our laboratory is Quality Certified under ISO 9001 regulations, works in compliance with GLP (Good Laboratory Practices) and has vast experience in the field of genetics with more than 6 years' experience and over 30,000 tests performed with complete satisfaction.

The genotyping technology we use is TaqMan® OpenArray® Real-Time CRP by Applied Biosystems for the DNA hybridization process and detection of target molecules tagged with nucleotide fluorescence during DNA synthesis. TaqMan® technology uses two 'Minor Groove Binder (MGB)' allele probes together with the associated amplification 'primers' as this results in high precision and reliable genotypes.

OpenArray® uses special nanoporated plates that enables up to 3,072 simultaneous reactions, thus simplifying the execution of a series of repetitions of each test and improving their reliability.

By combining both TaqMan® and OpenArray® technologies, we can provide genotyping of the highest quality **that is quick, safe and extremely reliable (99.9%)** with very small DNA samples.



## Genetics vs. Life style, which is most important?

Even though all human beings are genetically the same (99.9%), it is this 0.1% remaining which makes us different from each other and means what works for one person will not necessarily be effective for another. This is why we all respond differently to the same product, diet, exercise or ageing.

Alopecia is a gradual and multifactorial process that implies aesthetic changes in the body. When referring to its general definition, alopecia is determined by a series of intrinsic and extrinsic factors.

Intrinsic factors include genes and their expression. Alopecia is mainly inherited from our parents and family. It is therefore essential to understand our genes as our DNA contains basic information about our susceptibility to alopecia.

On the other hand, extrinsic factors may accelerate the development of alopecia as these factors influence our day to day activities. Constant changes in our life style like periods of stress and frenetic moments bring about situations that makes our bodies suffer. Hair loss suddenly increases during these anxious times.

The combination of genetic characteristics (genotype; intrinsic factors) and our life style (environment; extrinsic factors) creates a phenotype, that is, what we really are. Alopecia has various causes that must be approached as a whole in order to improve the health of our hair.

## 04 ANTI-ALOPECIA MEDICATIONS ANALYSED

### The personalised solution for your alopecia

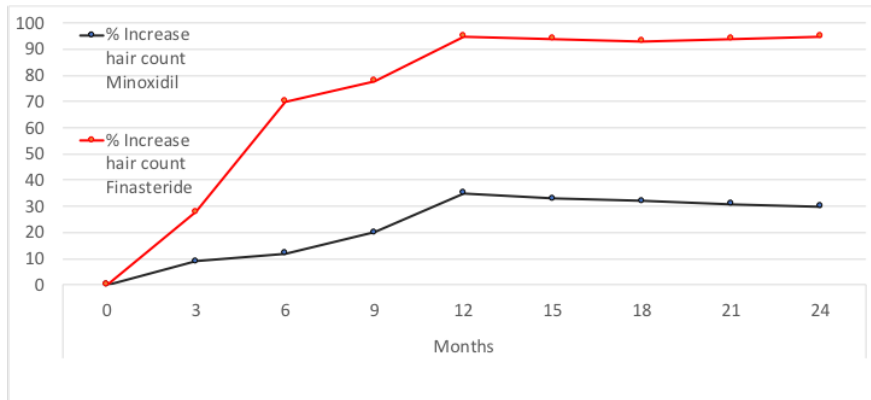
After analysing your DNA with its SNP or mutations related to the metabolic pathways of all anti-alopecia medications, we can determine which drugs will be the most effective, at which dose and which ones should be avoided.

### Metabolic pathways and compounds analysed:

<b>Anti-inflammatory</b>	<b>Antifungal</b>
Clobetasol propionate	Clotrimazole
Triamcinolone acetonide	Ketoconazole
Hydrocortisone	Metronidazole
Betamethasone dipropionate	<b>Prostaglandins</b>
Fluocinolone acetonide	Latanoprost Fagron
	Minoxidil
	Prostaquinon TM
	Cetirizine Hcl
<b>Keratolytic</b>	<b>Antipruritic</b>
Salicylic acid	Erythromycin
Tretinoin	<b>Minerals</b>
Urea	Oral Zinc sulfate
<b>Antioxidant</b>	<b>Antiandrogenic</b>
Selenium yeast	Dutasteride
Astaxanthin	17- $\alpha$ Estradiol
	Finasteride
	Melatonin
	Topical Saw Palmetto
	Saw Palmetto
	Spironolactone
<b>Circulation</b>	<b>Collagen synthesis</b>
Arginine	Oral SiliciuMax TM
L-Carnitine L-tartrate	Cystine
Ginkgo biloba	MSM
<b>Insulin-like growth factor increase</b>	<b>Vitamin deficiency</b>
IGrantine-F1 TM	Tocopherol (vit. E)
	Topical Biotin
	Oral Biotin
	Nicotinamide ( Vit B3)
	Pyridoxine HCl (Vit. B6)
<b>Softener</b>	
D-Panthenol	



By using the results of the test, your Physician can prescribe the ideal personalised treatment for your alopecia. In 70% of cases treated with this approach there is an improved treatment outcome and improved treatment efficacy.




Abir Saraswat, MD, DNB; Bhushan Kumar, MD, MNAMS1. Author Affiliations. Arch Dermatol. 2003;139(9): 1219-1221

## 05 PATIENT DATA

### Demographic data on the patient





**Gender** Female

**Age** 50 years

**Height** 178 cm

**Weight** 80 Kg

**BMI** 25,24

**Stress** No

**Suffers depression** No

**Sufficient rest** Yes

**Illnesses** No

**Intake** Tobacco

**Takes prescription drugs** No

**Known allergies to substances** No



## Hair loss data

Type of alopecia	Androgenic alopecia
Degree of alopecia on the scale	Grade 1B
Family history of alopecia	None
Time since beginning of hair loss	-1
Prescription testosterone derivatives	No

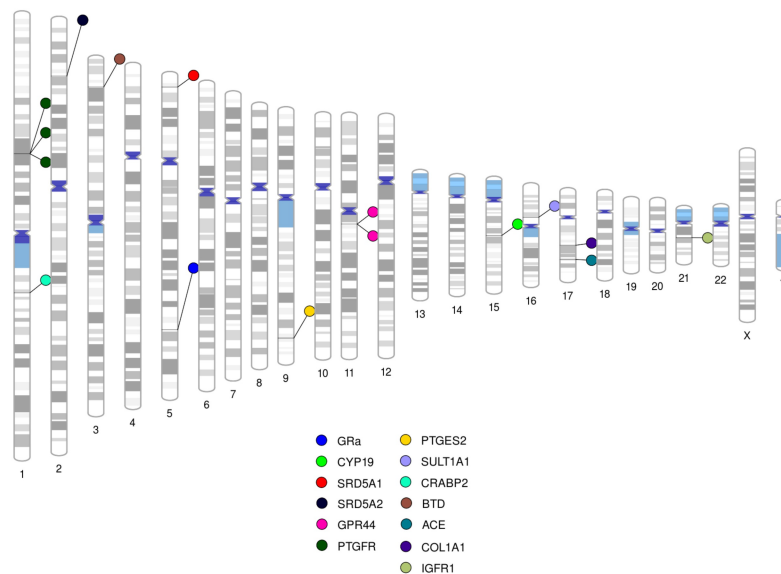
## Clinical examination results

Pull-Test	A lot
Complaints associated with alopecia	No
Patchy alopecia	No
Current anti-alopecia treatment	No
Previous anti-alopecia treatment	No

## 06 GENES AND VARIATIONS STUDIED

### Chromosomes and genes

The TrichoTest™ alopecia test studies a total of 48 genetic variations in 16 key genes to determine how alopecia affects you and to what extent. The chart below shows the location of the genes in the chromosomes of the human genome:



## 07 RESULTS ACCORDING TO YOUR GENETIC PROFILE

### Summary of the results

- Positive** : The genetic variation detected has a POSITIVE influence.
- Moderate** : The genetic variation detected has a MODERATE influence.
- Negative** : The genetic variation detected has a NEGATIVE influence.

Gene name	Description	Effect
<b>TREATMENT EFFICACY WITH PROSTAGLANDIN INHIBITORS</b>		
<b>GPR44-1</b>	Genetic result: Predisposition to slightly higher GPR44 mRNA stability. Interpretation: Prostaglandin D2 receptor 2 (GPR44 or CRTH2) variants are associated with an increased GPR44 mRNA stability leading to an increased responsiveness to prostaglandin D2 and hair follicle regression. Treatment/dosage: Treatment with prostaglandin D2 inhibitors (Cetirizine and/or Prostaquinon) at normal doses would be highly recommended.	
<b>GPR44-2</b>	Genetic result: Predisposition to slightly higher GPR44 mRNA stability. Interpretation: Prostaglandin D2 receptor 2 (GPR44 or CRTH2) variants are associated with an increased GPR44 mRNA stability leading to higher responsiveness to prostaglandin D2 and hair follicle regression. Treatment/dosage: Treatment with prostaglandin D2 inhibitors (Cetirizine and/or Prostaquinon) at normal doses would be highly recommended.	
<b>PTGFR-1</b>	Genetic result: Increased likelihood of having a positive response to Latanoprost. Interpretation: Prostaglandin F receptor (PTGFR) variants are related with Latanoprost treatment efficacy (prostaglandin analog) . Treatment/dosage: Treatment with Latanoprost at normal doses is recommended.	
<b>PTGFR-2</b>	Genetic result: Increased likelihood of having a positive response to Latanoprost. Interpretation: Prostaglandin F receptor (PTGFR) variants are related with Latanoprost treatment efficacy (prostaglandin analog) . Treatment/dosage: Treatment with Latanoprost at normal doses is recommended.	
<b>PTGFR-3</b>	Genetic result: Increased likelihood of not having a positive response to Latanoprost. Interpretation: Prostaglandin F receptor (PTGFR) variants are related with Latanoprost treatment efficacy (prostaglandin analog) . Treatment/dosage: Treatment with Latanoprost at normal doses is not recommended.	
<b>TREATMENT EFFICACY WITH MINOXIDIL</b>		
<b>PTGES2</b>	Genetic result: Predisposition to slightly reduced PGE2 levels. Interpretation: Prostaglandin E synthase 2 (PTGES2) variants are associated with lower prostaglandin E2 production (hair growth promoter). Treatment/dosage: Treatment with normal doses of Minoxidil to stimulate prostaglandin E2 would be recommended.	
<b>SULT1A1</b>	Genetic result: Predisposition to reduced SULT1A activity. Interpretation: Minoxidil Sulfotransferase Enzyme (SULT1A1) variants predict response to minoxidil treatment. Treatment/dosage: Minoxidil may be recommended but in high doses, with the aim of trying to ensure therapeutic activity.	

Positive

Moderate

Negative

Gene name	Description	Effect
<b>TREATMENT EFFICACY WITH GLUCOCORTICOID ANTI-INFLAMMATORIES</b>		
<b>GR-alpha</b>	Genetic result: Predisposition to normal sensibility to glucocorticoid anti-inflammatory treatments. Interpretation: Glucocorticoid Receptor (GR or NR3C1) variants are associated with resistance or sensitivity to corticosteroids. Treatment/dosage: SNP analysis indicates that normal doses of glucocorticoids should be effective.	
<b>TREATMENT EFFICACY WITH ANTIANDROGENICS</b>		
<b>CYP19A1</b>	Genetic result: Predisposition to reduced CYP19A1 activity. Interpretation: Aromatase (CYP19A1) variants are associated to low conversion of testosterone in estrogens and to high conversion into DHT (hair growth inhibitor). Treatment/dosage: Treatment with topical 17- $\alpha$ Estradiol (aromatase inducer) at normal doses is recommended.	
<b>SRD5A1</b>	Genetic result: Predisposition to increased SRD5A1 activity leading to increased DHT levels. Interpretation: Steroid 5 $\alpha$ -Reductase 1 (SRD5A1) variants are associated with increased SRD5A1 activity leading to increased DHT levels and hair growth inhibition. Treatment/dosage: Treatment with Dutasteride at high doses is recommended.	
<b>SRD5A2</b>	Genetic result: Predisposition to increased SRD5A2 activity leading to increased levels of DHT Interpretation: Steroid 5 $\alpha$ -Reductase 2 (SRD5A2) variants are associated with increased SRD5A2 activity leading to increased DHT levels and hair growth inhibition. Treatment/dosage: Treatment with Finasteride at normal doses is recommended.	
<b>VASODILATATION AND BLOOD CIRCULATION</b>		
<b>ACE</b>	Genetic result: Predisposition to an increased Angiotensin conversion activity. Interpretation: Angiotensin-converting enzyme (ACE) variants are associated with increased plasma levels of angiotensin 2, an extremely potent vasoconstrictor. Treatment/dosage: Normal doses of circulation stimulators are recommended, such as Minoxidil, caffeine, Ginkgo biloba, Ginseng or Arginine.	
<b>COLLAGEN SYNTHESIS</b>		
<b>COL1A1</b>	Genetic result: Predisposition to normal collagen stability. Interpretation: Collagen, type I, alpha 1 (COL1A1) variants are associated with collagen instability. Treatment/dosage: SNP analysis does not indicate the necessity to supplement with hair strengthening composites.	
<b>VITAMIN A METABOLISM</b>		
<b>CRABP2</b>	Genetic result: Predisposition to normal retinoic acid intracellular transport. Interpretation: Cellular retinoic acid-binding protein 2 (CRABP2) variants are associated with lower retinoic acid (vitamin A) intracellular transport. Treatment/dosage: SNP analysis does not indicate the necessity to supplement with vitamin A.	

Positive

Moderate

Negative

Gene name	Description	Effect
<b>BIOTIN METABOLISM</b>		
<b>BTD</b>	Genetic result: Predisposition to normal biotinidase activity. Interpretation: Biotinidase (BTD) variants are associated with low biotin (vitamin B7) uptake from the diet. Treatment/dosage: SNP analysis does not indicate the necessity to supplement with vitamin B.	
<b>REDUCTION OF IGF-1 LEVELS</b>		
<b>IGF1R</b>	Genetic result: Predisposition to normal IGF-1 levels. Interpretation: Insulin-like growth factor-I (IGF-I) variants are associated with lower plasma IGF-1 levels leading to hair loss. Treatment/dosage: SNP analysis does not indicate the necessity to treat with IGF-1 inducers.	

## The best products for your scalp

After analysing your DNA and life style, we create your profile. The compilation considers all your strengths and weaknesses and how you are affected by your alopecia and to what degree. As a result of the information available, we have selected exclusive compounds that will help you combat alopecia. The following colour scale shows what we most recommend (the intensity of the green indicating from more to less recommended) and those compounds we do not recommend (from white to red, indicating less recommended).

<b>Anti-inflammatory</b>		<b>Antiandrogenic</b>	
Betamethasone dipropionate	Red	Dutasteride	Light Green
Clobetasol propionate	Red	Saw Palmetto	Light Green
Hydrocortisone	Red	17- $\alpha$ Estradiol	Light Green
Triamcinolone acetonide	Red	Finasteride	Light Green
Fluocinolone acetonide	Red	Topical Saw Palmetto	Light Green
		Melatonin	Light Green
<b>Antioxidant</b>		<b>Circulation</b>	
Astaxanthin	Light Green	Ginkgo biloba	Light Green
Selenium yeast	Light Green	Arginine	Light Green
		L-Carnitine L-tartrate	Light Green
<b>Collagen synthesis</b>		<b>Insulin-like growth factor increase</b>	
Oral SiliciuMax TM	White	IGrantine-F1 TM	White
Cystine	White		
MSM	White		
<b>Minerals</b>		<b>Keratolytic</b>	
Oral Zinc sulfate	Light Green	Tretinoin	White
<b>Softener</b>		<b>Prostaglandins</b>	
D-Panthenol	Light Green	Prostaquinon TM	Light Green
		Minoxidil	Light Green
		Cetirizine Hcl	Light Green
		Latanoprost Fagron	Light Green
		<b>Vitamin deficiency</b>	
		Oral Biotin	White
		Topical Biotin	White
		Nicotinamide ( Vit B3)	White
		Pyridoxine HCl (Vit. B6)	White
		Tocopherol (vit. E)	White

## 08 ANALYSIS OF ALL THE METABOLIC PATHWAYS INVOLVED

A summary of your **genetic results** is shown below. We analyse the metabolic pathways related to anti-alopecia drugs: *the prostaglandin metabolism, inflammation and immune response, DHT metabolism, vasodilatation and blood circulation, collagen synthesis, vitamin metabolism and insulin metabolism.*

### 08.1 PROSTAGLANDIN METABOLISM

#### Why is it important?

Prostaglandins (PG) are a family of hormones that have various functions in our body such as: participation in the inflammatory response, regulation of gastric mucus and gastric acid, smooth muscle contraction, regulation of body temperature and control over blood pressure. Amongst these hormones the variants PGD<sub>2</sub>, PGF and PGE have been described as factors in hair loss due to their interaction with prostaglandin receptors (GPR44, PTGFR) and regulators (PTGES2 and SULT1A1).

<b>GPR44 (Prostaglandin receptor)</b>
<i>What is this gene?</i>
The GPR44 gene encodes the receptor for various prostaglandins E <sub>2</sub> , with variable affinities depending on: PGD <sub>2</sub> >> PGF <sub>2</sub> α = PGE <sub>2</sub> > PGI <sub>2</sub> = thromboxane A <sub>2</sub> .
<i>Why do we analyse it?</i>
<ul style="list-style-type: none"><li>• When the GPR44 receptor binds the prostaglandins (especially PGD<sub>2</sub>) it triggers a series of reactions and genetic activations which, apart from regulating inflammation and cell cycles also gives rise to increased hair loss.</li><li>• The variation analysed in this test indicates the potential lesser stability of the mRNA receptor, giving rise to a possible lower concentration or less effectiveness of these receptors in the cells and therefore, less activation of pathways that cause hair loss.</li></ul>
<i>What do we analyse and what incidence does it have in our population?</i>
This test analyses the two GPR44 mutations with the greatest expected incidence among populations. The presence of one or two copies of risk allele G in the first variant is estimated at ~70% of the population. On the other hand, in the second variant, the presence of one or two copies of risk allele C is estimated at ~62% of the population.

<b>PGTFR (Prostaglandin receptor F)</b>
<i>What is this gene?</i>
PTGFR (Prostaglandin F Receptor) is the gene that encodes the main cell receptor for prostaglandin F2 (PGF2&alpha). In a similar way to GPR44, analysed above, it has variable affinity depending on: PGF2α > PGD2 > PGE2
<i>Why do we analyse it?</i>
<ul style="list-style-type: none"> <li>• This gene is expressed in the dermal papilla and is associated with increased hair loss or less hair regeneration. Compounds such as Latanoprost demonstrated an inhibitory effect on alopecia in association with PGTFR.</li> </ul>
<i>What do we analyse and what incidence does it have in our population?</i>
<p>We analyse a series of genetic variations closely related to the probability of obtaining a successful response in the treatments with compounds such as Latanoprost. The mean expected incidence of the risk alleles among the population is:</p> <ul style="list-style-type: none"> <li>• rs6686438 - T - 36%</li> <li>• rs1328441 - A - 54%</li> <li>• rs10782665 - G - 37%</li> </ul>

<b>PTGES2 (Prostaglandin E2 Synthase)</b>
<i>What is this gene?</i>
The PTGES2 gene encodes prostaglandin E2 synthase, converting PGH2 into the stable PGE2 form.
<i>Why do we analyse it?</i>
<ul style="list-style-type: none"> <li>• It is well known that any reduction in the levels of prostaglandin E2 induces situations prone to alopecia. Together with other prostaglandins, PTGES2 is one of the main targets in hair loss treatments.</li> <li>• The variation analysed in the gene that synthesises PGE2 gives rise to reduced enzymatic activity that results in a lower concentration of available PGE2, therefore giving rise to a situation prone to alopecia.</li> <li>• Hair treatments such as Minoxidil concentrate on this metabolic pathway, aiding increased PGE2 levels.</li> </ul>
<i>What do we analyse and what incidence does it have in our population?</i>
We analyse the genetic variant rs13283456 of the PTGSE2 gene, with an expected incidence of its risk allele T of ~40%.

<b>SULT1A1 (Sulfotransferase 1A1)</b>
<i>What is this gene?</i>
SULT1A1 encodes a sulphotransferase enzyme that is responsible for modulating excretion as well as the functional activation of some compounds in the body.



*Why do we analyse it?*

- It has been scientifically demonstrated that certain genetic variations give rise to a SULT1A1 enzyme with a greater or lesser functional rate.
- Minoxidil is one of the compounds activated by SULT1A1. By determining the enzyme activation rate, we can gain indications of the need or otherwise of modulating the dose for the treatment of alopecia.

*What do we analyse and what incidence does it have in our population?*

This study analyses the SULT1A1\*2 genotype where the presence of allele T indicates a lower rate of Minoxidil activation. This is estimated in about 25% of the population.

## 08.2 INFLAMMATION AND AUTOIMMUNE RESPONSE

### Why is it important?

Clobetasol Propionate is a synthetic fluorinated corticosteroid for topical use. Clobetasol is used to alleviate inflammation and itching associated with alopecia. Clobetasol is a very powerful topical corticosteroid and is therefore capable of having systemic glucocorticoid effects.

#### **GR- $\alpha$ (Glucocorticoid receptor $\alpha$ )**

*What is this gene?*

The GR gene encodes the glucocorticoid receptor and its primary function is to regulate the signalling of this metabolic pathway. The GR gene acts as a transcription factor for genes that respond to glucocorticoids. These genes include regulators of inflammatory processes, cell proliferation and differentiation depending on the tissue. Mutations in this gene have been associated with resistance or sensitivity to corticosteroids.

*Why do we analyse it?*

- Corticosteroid compounds are one of the most widely used remedies to treat inflammation. Their effectiveness however is known to be highly variable and even unpredictable to a certain extent.
- Polymorphisms in the glucocorticoid receptor (GR) have been involved in the variability of the response generated to corticosteroid compounds.
- Polymorphisms in the human gene GR- $\alpha$  (hGR  $\alpha$ ), the biologically active form, enables us to define the response to treatment profile, the possible required dose and the resistance or sensitivity to corticosteroids.

*What do we analyse and what incidence does it have in our population?*

Analysis of the A3669G variant of GR, a mutation that affects the mRNA stability and results in over-production of the inactive form of the protein. It has been determined that this mutation reduces GR induced signalling.

The expected incidence of the presence of risk allele G is estimated at between 20% and 40%.

## 08.3 DHT METABOLISM (DIHYDROTESTERONE)

### Why is it important?

Dihydrotestosterone is also called DHT, 5 $\alpha$ -Dihydrotestosterone, 5 $\alpha$ -DHT or Androstanolone. This hormone is an androgen and an active biological metabolite of the hormone Testosterone. DHT is mainly synthesised in the prostate, testicles, hair follicles and suprarenal capsules by the enzyme 5 $\alpha$ -reductase. This enzyme reduces the double 4,5 bond of Testosterone.

<b>CYP19 (Aromatase)</b>
<i>What is this gene?</i>
The CYP19 gene, located in chromosome 15q21.1, encodes the aromatase enzyme. This gene also encodes a member of the Cytochrome P450 enzyme superfamily. Cytochrome P450 proteins are mono-oxygenases and their function is catalysis of some reactions in the synthesis of cholesterol, steroids and other lipids. This protein is found in the endoplasmic reticulum of the cell and catalyses the final steps of estrogen biosynthesis (including oestrone and oestradiol).
<i>Why do we analyse it?</i>
<ul style="list-style-type: none"><li>• Mutations in Cyp19 aromatase have been associated with a reduction or increase of the enzyme activity rate, giving rise to unbalanced levels of oestradiol/testosterone in serum.</li><li>• It is likely that testosterone concentrations are increased in the presence of aromatase enzymes with a low activity rate. In this situation the function of 5-alpha-reductase, the enzyme that transforms testosterone into DHT, is promoted. DHT is notorious for causing hair loss.</li></ul>
<i>What do we analyse and what incidence does it have in our population?</i>
Analysis of the 15658C>T mutation of CYP19, with presence of the risk allele has been associated with lower aromatase activity rates. The expected incidence of the presence of risk allele T is estimated at between 47% and 50%.

<b>SR5DA (Steroid 5<math>\alpha</math>-reductase)</b>
<i>What is this gene?</i>
The SRD5A gene encodes an isoform of the steroid 5-alpha-reductase enzyme, responsible for catalysing the conversion of testosterone to a more powerful androgen called dihydrotestosterone (DHT).
<i>Why do we analyse it?</i>
<ul style="list-style-type: none"><li>• A high 5-alpha-dihydrotestosterone production means that it is accumulated in the hair follicles thus increasing their telogen cycle causing faster hair loss and atrophying hair follicles.</li><li>• The mutation analysed has been associated with an unbalanced dihydrotestosterone/testosterone ratio. This means that the presence of genetic allele C marks a greater tendency to high DHT levels.</li></ul>
<i>What do we analyse and what incidence does it have in our population?</i>
Analysis of the 116C>G mutation of the SRD5A1 enzyme whose incidence is estimated at between 40-45% as well as analysis of the V89L mutation of the SRD5A2 enzyme whose incidence is estimated at 35%.

## 08.4 VASODILATATION AND BLOOD CIRCULATION

### Why is it important?

Vasoconstriction is a potent cause of alopecia, therefore knowing the genetic profile for a tendency to high blood pressure could aid in the selection of treatments to increase vasodilatation and blood circulation.

<b>ACE (Angiotensin I)</b>
<i>Why is it important?</i>
The angiotensin converting enzyme I (ACE) plays a key role in blood pressure regulation. ACE converts inactive angiotensin I into its active form angiotensin II. Angiotensin II is a potent vasoconstrictive agent and this means that when it bonds to its receptor the blood vessels contract, thereby increasing blood pressure.
<i>Why do we analyse it?</i>
<ul style="list-style-type: none"><li>• There are two forms of ACE produced by changes in the genetic code of the gene, ACE I and ACE D, which correspond to insertion (I) or deletion (D) of a short section of DNA within the gene.</li><li>• People with allele I typically show reduced ACE activity in comparison to those with allele D.</li><li>• Vasoconstriction is a potent cause of alopecia, therefore knowing the genetic profile for a tendency to high blood pressure could aid in the selection of treatments to increase vasodilatation and blood circulation.</li></ul>
<i>What do we analyse and what incidence does it have in our population?</i>
The G2328A genetic variation of ACE is also analysed. The risk allele G has a populational incidence of about ~46% and gives rise to increased blood pressure.

## 08.5 COLLAGEN SYNTHESIS

### Why is it important?

This protein is an important component of hair and so any deficiency may cause hair to break or be dull.

<b>COL1A1 (Type 1 collagen)</b>
<i>Why is it important?</i>
The COL1A1 gene encodes the major compound of type 1 collagen which is present in the majority of connective tissues (supporting tissues), including cartilage.

#### *Why do we analyse it?*

- COL1A1 is involved in collagen synthesis and therefore in the strength, firmness and capacity to sustain the body in general.
- The presence of the risk T allele is closely associated with an increase in the tendency to develop bone problems, as well as with a clear increase in ageing of the skin and connective tissues
- The most visible symptoms are wrinkles and flaccidness, hair loss, fragile nails and more tangible and concerning, joint pain, bone fractures and premature osteoporosis, both clear symptoms of premature ageing.

#### *What do we analyse and what incidence does it have in our population?*

In this test we analyse the best known mutation, 1546G>T, with an expected incidence of about 20% in the population.

## 08.6 VITAMIN METABOLISM

### Why is it important?

Vitamin A contributes to the creation of retinoids that stimulate hair follicles and reinforce the production of new hair. Foods such as chards, spinach or carrot contain abundant Vitamin A. Vitamin B nourishes hair follicles. The Group B vitamins also aid in combating stress (one of the main causes of hair loss).

#### **CRABP<sub>2</sub> (Cellular Retinoic Acid Binding Protein 2)**

##### *Why is it important?*

The CRABP2 gene encodes a protein responsible for transporting retinoic acid or Vitamin A to cell sites and is closely related to cell differentiation in epithelial tissues.

##### *Why do we analyse it?*

- It is well-known that under certain circumstances treatment with Minoxidil should be supplemented with retinoic acid to increase its efficacy. In cases, for example, of a SULT1A1 genotype (analysed above) not favourable to Minoxidil, an analysis of the CRABP2 result could be recommendable.
- Genetic variations in CRABP2 have been associated with an increase in the Vitamin A concentration in serum, giving rise to a lower intracellular transport rate and therefore reducing the efficacy of treatments with retinoic acid.

##### *What do we analyse and what incidence does it have in our population?*

We analyse the rs12724719 variant of the CRABP2 gene. The presence of allele A determines less efficacy of the protein. The incidence of allele A is estimated at 20% of the population.

<b>BTD (Biotinidase)</b>
<i>What is this gene?</i>
The BTD gene provides instructions for the manufacture of an enzyme called biotinidase. This enzyme recycles biotin, a vitamin B found in foods such as liver, egg yolks and milk. Biotinidase absorbs the biotin in food and releases the vitamin in its free state.
<i>Why do we analyse it?</i>
<ul style="list-style-type: none"> <li>• The body needs free biotin to activate enzymes called biotin-dependent carboxylase. These carboxylases are involved in many critical cell functions.</li> <li>• Any genetic variation analysed enables determining whether our body needs additional biotin.</li> <li>• A vitamin B deficiency has been associated with progressive hair loss.</li> </ul>
<i>What do we analyse and what incidence does it have in our population?</i>
We analyse the rs13078881 variation (c.1330G>C, p.Asp444His) with a populational incidence of the risk C allele of about 5%.

## 08.7 **INSULIN-LIKE GROWTH FACTORS**

### **Why is it important?**

It has been observed that people with higher insulin resistance (mutated insulin receptors), are more likely to develop alopecia.

<b>IGFR-1 (Insulin-like growth factor 1 receptor)</b>
<i>What is this gene?</i>
The IGFR-1 gene encodes a protein that is found on the surface of the cells, acting as a receptor of the IGF-1 hormone (a molecule with a similar structure to the insulin), responsible for cell growth.
<i>Why do we analyse it?</i>
<ul style="list-style-type: none"> <li>• The levels of IGF-1 decrease substantially in areas where the hair loss is more aggressive, and these are controlled by androgenic factors.</li> <li>• In some adults the levels of IGF1 are lower than expected because of a genetic variation in the IGFR-1 receptor.</li> <li>• Knowing if you are predisposed to lower levels of circulating IGF-1 will give rise to a possible increase in the effectiveness of those treatments focused on increasing the levels of IGF-1</li> </ul>
<i>What do we analyse and what incidence does it have in our population?</i>
In this test we analyse the rs222976 mutation of the IGFR-1 gene. There is an expected presence of around 20% alleles AA in the population.
<i>What can we do if we detect the mutation?</i>
<p>If we detect the presence of the allele A, it is recommended to incorporate active ingredients in the hair treatment which are aimed at increasing the levels of available IGF-1.</p> <p>The expected effectiveness of the treatment should be greater as a result of the innate need for the person to increase the levels of IGF-1. In addition, it is reasonable to suggest that the dosage in people with the AA mutation should exceed that of those with genotype AG and GG.</p>

## 09 RECOMMENDATIONS

Closely follow the treatment indicated by your doctor for best results.

Some general recommendations:

1. Use a hair loss shampoo with essential oils that soothe and moisturise the scalp and increase hair thickness.
2. Use a conditioner that moisturises and gives the hair greater volume.
3. Once or twice a week, 10 minutes before washing the hair, nourish the scalp with hair oil.
4. Avoid eating sweet or fatty foods.
5. Drink a lot of water to keep the body hydrated, including the scalp and hair.
6. If you have long hair, avoid over tightening pony-tail or plaits. In addition, avoid as far as possible using hats that continually rub the scalp and prevent the hair from contact with the air.
7. When using a hair-dryer, do not hold it close to your head as the heat quickly dries out hair leaving it brittle and prone to loss.
8. Direct sunlight on your head is also detrimental so, whenever possible, use a scarf or hat to protect your scalp from the sun.
9. Avoid hair lacquers and sprays as far as possible, as they contain substances that are aggressive to your hair.
10. Hair serums that close the cuticle and nourish hair, giving it more volume, are highly recommended.

## 10 GLOSSARY

### **NUCLEIC ACID**

The basic unit of nucleic acids. An organic compound comprised of a nitrogen base, a sugar and a phosphate group.

### **DNA**

Deoxyribonucleic acid composed of two chains and which contains the genetic information for the growth, division and function of a cell.

### **AMINO ACID**

Basic unit of proteins encoded by a codon and bonded together by peptide links. The molecule consists of a basic amino group (NH<sub>2</sub>), a carboxylic group (COOH), a hydrogen atom (-H) and a lateral organic group (R) bonded to the carbon atom, which varies for each amino acid.

### **RNA**

Abbreviation for ribonucleic acid which generally has a single chain (a double chain in some virus) and is responsible for transferring information from the DNA to the system for forming cell proteins.

### **BIOINFORMATICS**

The science of information technology applied to biological research.

### **BIOTECHNOLOGY**

The application of biological organisms, systems or processes to determine the science of life and improve the value of materials and organisms, including pharmaceutical products, crops and livestock. It is a relatively new, fast developing science that incorporates knowledge from various traditional sciences: biochemistry, chemistry, microbiology and chemical engineering

### **CELL**

The structural, functional and biological unit of every organism. An individual unit that can exist as an independent functional life unit (such as in the case of unicellular organisms), or as a subunit of a multicellular organism (for example, plants and animals, multicellular organisms). It is specialised in performing particular functions that serve the purpose of the organism as a whole.

### **GENETIC CODE**

Relationship between the sequence of bases in nucleic acid and the order of the amino acids in the polypeptide synthesised from this acid. A sequence of three nucleic acid bases (a triplet) acts as a code word (codon) for an amino acid.

### **CHROMOSOME**

The structure inside the cell that contains genetic material as a linear chain of DNA bonded to various proteins in the nucleus of eukaryote cells, or as a circular chain of DNA (or RNA in some virus) in the cytoplasm of prokaryotes and in the mitochondria and chloroplasts of some eukaryotes.

### **EPIGENETICS**

Science that studies hereditary phenotypes that are stable as a result of changes in a chromosome without disorders in the DNA sequence.

### **PHENOTYPE**

Physical or biological aspect that characterises an organism as a result of the interaction between its genotype and the environment.



## **GENE**

A gene is the basic physical unit of heredity. Genes are transmitted from parents to their children and contain the information necessary to specify their characteristics. Genes are organised, one after the other, in structures called chromosomes. It is the basic physical and functional unit of heredity.

## **HUMAN GENOME**

The genome of Homo Sapiens is comprised of 24 different chromosomes (22 autosomal pairs and one pair of sex chromosomes) with a total of about 3 thousand million pairs of DNA bases estimated to contain close to 20,000-25,000 genes.

## **MICROARRAY**

Small solid tray, generally a membrane, where the DNA sequences are established in a specific order. DNA microarrays are used to detect the expression and / or sequence of many genes at the same time.

## **MUTATION**

A permanent inheritable change in the nucleotide sequence of a gene or chromosome.

## **PROTEIN**

Molecule comprised of amino acid polymers bonded by peptide links. Fats and carbohydrates can be differentiated by the nitrogen they contain. Other components include carbon, hydrogen, oxygen, sulphur and sometimes phosphorous.

## **SNP**

Variation in the DNA sequence that occurs when a single nucleotide (A, T, C or G) is altered in the genome sequence. Each individual has many single nucleotide polymorphisms that combine to form a DNA pattern that is unique to this person.

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