ELIPSEgenes

Basic preventive profile

Surname:	Ejemplo	**Reception date:**	DD/MM/YYYY
Name:	Paciente Modelo	**Validation date:**	DD/MM/YYYY
Birth Date:	DD/MM/YYYY	**Sample Type:**	-
ID nr:	-	**Physician:**	-
Gender:	Male		
Order:	-	**Validation by:**	-

Objective of this profile

The purpose of this profile is to study polymorphisms in certain genes that are known to influence the absorption, metabolism or action in the therapeutic target of nutrients and trace elements. Its practical application is to recommend personalized nutritional habits to improve health and prevent certain pathologies.

Lipid metabolism

Polymorphisms related to genetic vascular risk. Their knowledge allows us to adjust the amount and type of fats in diet.

Carbohydrates metabolism

There are polymorphisms in certain genes associated with carbohydrate metabolism that influence the risk of obesity and insulin resistance or diabetes.

Genetic diseases

Lactose intolerance, celiac disease and hemochromatosis are common genetic diseases and in many cases their symptoms are of late onset. Their detection allows preventive treatment, with or without symptoms, to avoid their onset.

Caffeine and alcohol removal

Moderate levels of caffeine exert a positive action on wakefulness, but high levels can cause anxiety and increase cardiovascular risk.

Vitamin action

Certain polymorphisms in the metabolism of vitamin B or vitamin D receptor, may cause that normal intake levels of these vitamins, be insufficient in a nutritional effects.

Functional hypothyroidism

A polymorphism in DIO2 gene may affect the conversion of T4 to T3 in tissues. In those affected, clinical signs of hypothyroidism may appear, despite having normal levels of T4 and T3 in serum.

Inflammation

There are polymorphisms that are related to a higher or lower expression of synthesis of antiinflammatory and/or proinflammatory interleukins.

Appetite control

Polymorphisms in two genes that control the sensations of appetite and satiety, can influence the intake habits of each person.

Selected genetic polymorphisms

Below are the genetic variants studied for this report. Depending on the results, nutritional and lifestyle recommendations are given, and are adapted to your profile. It is essential that, before taking any **nutritional supplement together with medication, you consult your doctor** to **avoid adverse reactions** to the medication.

Gene	Rs identifier	Polymorphism	Results
6p21 (DQ2.5)	rs2187668	C>T	CC
6p21 (DQ8)	rs7454108	T>C	TT
ADH1B	rs1229984	His48Arg	CC
ADORA2	rs5751876	1976T>C	TT
ADRB2	rs1042713	Arg16Gly	AA
ALDH2	rs671	42076G>A	GG
APOA1	rs670	-75G>A	CC
APOA5	rs662799	T1131C	AA
APOC3	rs5128	rs5128 (C>G)	CG
APOE	rs429358 + rs7412	112/158	E3/E3
COMT	rs4680	Val158Met	Val/Met
CYP1A2	rs2069514	*1C	wt/wt
CYP1A2	rs762551	*1F	*1F/*1F
CYP2R1	rs10741657	-1127T>C	AG
DIO2	rs225014	Thr92Ala	CT
FABP2	rs1799883	Ala54Thr	CC
FTO	rs9939609	rs9939609 (T>A)	TT
GHRL	rs696217	Leu72Met	GG
HFE	rs1800562	Cys282Tyr	GG
HFE	rs1800730	Ser65Cys	AA
HFE	rs1799945	His63Asp	CC
IL10	rs1800896	-1082G>A	TT
IL1A	rs1800587	-889G>A	AG
IL1B	rs1143634	315C>T	GA
IL6	rs1800795	-174C>G	GG
LCT	rs4988235	-13910C>T	CC

Gene	Rs identifier	Polymorphism	Results
LEP	rs13245201	1414G>A	AG
LEPR	rs1137100	rs1137100(A>G)	AG
MTHFR	rs1801133	677C>T	GA
PPARG	rs1801282	P12A	CC
TNFa	rs1800629	-308G>A	AG
VDBP	rs7041	1296 T>G	AA
VDR	rs1544410	BsmI	CT

Risk | Normal | Protective

Lipid metabolism

Cardiovascular diseases affect the arteries of the heart and blood vessels of the rest of the body, mainly the brain, kidneys and lower extremities. The most important are: myocardial infarction and cerebrovascular accident (thrombosis, embolism and cerebral hemorrhage). They are very serious and represents the leading cause of death in developed countries.

The cardiovascular risk factors are classified into 2 large groups:

• **Modifiable factors:** factors on which correct measures can be taken to avoid them such as hypertension, high cholesterol, metabolic syndrome and diabetes, obesity, smoking, sedentary lifestyle, alcohol abuse, anxiety and stress.
• **Non-modifiable factors:** factors that cannot be avoided such as age, sex, race, and family history, ie genetic factors.

In this section we study the most relevant genetic variants due to their influence on the risk of triglycerides and high cholesterol.

Gene	Rs identifier	Polymorphism	Results
APOA1	rs670	-75G>A	CC
APOA5	rs662799	T1131C	AA
APOC3	rs5128	rs5128 (C>G)	CG
APOE	rs429358 + rs7412	112/158	E3/E3
PPARG	rs1801282	P12A	CC

Consequences

The detected genotype in the studied genes, considered globally, is related to a **less favourable lipid metabolism** compared to the majority of the population.

The detected genotype of the **APOE** gene is associated with variant **E3/E3.** This genotype has not correlation neither positive nor negative on cardiovascular. This variant is related with the risk of the general population. A personalised diet allows the risk to be optimised.

Recommendations

• **Avoid** excessive **calorie** consumption and **reduce overweight** and **obesity**, since they are a cardiovascular risk factors. Maintain an adequate BMI (Body Mass Index).

• **Include** foods rich in **Polyunsaturated Fatty Acids (omega 3 and 6)** from, fish, nuts, seeds or vegetable oils.

• **Include** in the diet **Monounsaturated Fatty Acids (omega 9)** such as avocado or olive oil. The diet should contain about 14 gr of MUFA.

• **Limit saturated fats** to less than 7% of your total daily calories and **exclude trans fats** from fried, processed and ultra-processed foods, such as baked goods.

• **Reduce** the consumption of **refined carbohydrates** (pasta, rice, white flours...) and prefer wholemeal carbohydrates.

• **Avoid** foods rich in **refined sugars** such as candies, fruits in syrup, jams, pastries, sliced bread, cookies...

•**Increase**consumption of**Vitamin B3**(**niacin**) present in lean meats, fish, nuts, eggs, fruits and vegetables, whole grains, yeast and wheat germ.

• **Opt** for a nutrition rich in **fiber**. Preferably consume 25-30 g/day of fiber.

• **Avoid alcohol** consumption.

• **Practice regular physical activity** (at least 150 minutes per week of moderate-intensity exercise).

Due to APOE3/E3 genotype, is recommended to follow a diet with the following composition:
• 25% fat: prioritize **monounsaturated** and **polyunsaturated fat**. Avoid trans fats.
• 20% proteins: preference of **vegetable origin**.
• 55% carbohydrates: complex carbohydrates of **low glycemic index** and **high fiber** content.

From an exercise point of view, **50% aerobic and 50% anaerobic** are recommended.

Carbohydrate metabolism

Type 2 diabetes is a **metabolic disorder** characterized by **elevated blood glucose levels** due to altered insulin production or utilization.

Insulin is necessary for the **transport of glucose** from the blood into the cells, where it is stored for use when needed.

Patients with type 2 diabetes have cells in different tissues (adipose, hepatic and muscular) that do not respond correctly to insulin. This phenomenon is called **insulin resistance**. It is characterized by the lack of absorption of glucose by the cells, which leads to **hyperglycemia**. High concentrations of glucose in the blood cause an increase in the **secretion of insulin** at the level of the **pancreas**, which however is not sufficient to cover the needs of the body.

People who are overweight are more likely to develop insulin resistance, because fat tissue interferes with the body's ability to use insulin properly. In general, type 2 diabetes develops gradually. **Life habits** must be taken into account, but also family history since **genetic inheritance** plays an important role in the development of this disease.

Gene	Rs identifier	Polymorphism	Results
FABP2	rs1799883	Ala54Thr	CC
FTO	rs9939609	rs9939609 (T>A)	TT
LEPR	rs1137100	rs1137100(A>G)	AG
PPARG	rs1801282	P12A	CC

Consequences

The detected genotype for the **FABP2** gene is related to normal absorption of fatty acids. It is also associated with lower rates of obesity, plasma triglyceride levels and lower risk of type 2 diabetes.

The detected genotype for the **FTO** gene is related to a lower risk of developing obesity and type 2 diabetes.

The detected genotype for the **LEPR** gene is related to a leptin receptor dysfunction that can lead to increased levels of leptin in the blood. It predisposes to insulin resistance, type 2 diabetes and metabolic syndrome. This risk is increased if there are low concentrations of omega-3 and high levels of arachidonic acid (omega-6).

The detected genotype for the **PPARg** gene is the most frequent in the population. However, in a context like the current one, where the majority of the population consumes a large amount of sugars, association studies relate the presence of the C allele (proline) with an increased susceptibility to develop insulin resistance, type 2 diabetes and metabolic syndrome.

Recommendations

• **Reduce simple sugars** such as white, cane or brown sugar, fructose, honey, candy, chocolate, molasses, syrups (corn, maple, malt, rice), jellies, jams and sweetened drinks.

• **Substitute "whites"** (pasta, rice and white flour...) with wholemeal carbohydrates.

• **Avoid diet products** since they substitute glucose with high levels of fructose or sweeteners that affect the intestinal microbiota.

• **Increase fiber intake**. The soluble fiber as the Psyllium reduce the increase of the glycemia.

• **Reduce** the consumption of **saturated fats, eliminate trans fats** and prefer a diet rich in **omega 9 monounsaturated** and omega 3 and 6 **polyunsaturated** fatty acids.

• **Avoid salt in excess** as it can cause hypertension, may reduce insulin sensitivity, and contribute to the development of type 2 diabetes.

• **Practice moderate-intensity** aerobic physical activity.

Caffeine elimination

The **caffeine** molecule is structurally similar to adenosine, so it binds to adenosine receptors present on the surface of cells without activating them, acting as a competitive inhibitor. Many tissues have adenosine receptors that are associated with **fatigue and sleep**, thus **stimulating wakefulness and helping to fix attention**.

The **effects of caffeine** on these receptors can be **positive**, but they can also be **harmful** to health. Epidemiological studies show that the **risk of caffeine on cardiovascular health follows a "J" curve**. That is, moderate intakes are preventive, but **high intakes increase anxiety and cardiovascular risk**.

The maximum recommended intake of caffeine is 400mg/day. But with a normal intake, there are people who, due to genetic polymorphisms, mainly in the genes **CYP1A2** and **COMT**, eliminate caffeine slower than normal, and in them **a "normal" intake can be harmful**.
Polymorphisms of the **ADORA2 gene**, encoding the adenosine receptor, can influence the appearance of **anxiety** with the **consumption of caffeine** and also on the **risk of arthritis** and the response to a treatment with methotrexate.

CAFFEINE CONTENT IN BEVERAGES:

Espresso: 80 mg	"American" coffe: 100 mg	Decaffeined coffee: 2-15 mg
Black tea: 50 mg	Green tea: 30 mg	Canned tea: 20 mg
Cola drink: 40 mg	"Energy" drinks.	Very variable: 50-250 mg

Gene	Rs identifier	Polymorphism	Results
ADORA2	rs5751876	1976T>C	TT
COMT	rs4680	Val158Met	Val/Met
CYP1A2	rs2069514	*1C	wt/wt
CYP1A2	rs762551	*1F	*1F/*1F

Consequences

The genotype detected for the **CYP1A2** gene is associated with increased enzymatic activity, resulting in increased caffeine elimination.

The genotype detected for the **ADORA2** gene is associated with an increased risk of developing anxiety after consuming caffeine (100mg). However, in a habitual high consumption of caffeine (300-400 mg/day) tolerance is generated and this effect is not observed. But in this case, this high consumption of caffeine will not produce a stimulating effect, since for the patient it will be equivalent to his "baseline level".

Recommendations

• It is important **not to take caffeine along with COMT or CYP1A2 inhibitors** such as resveratrol, naringine, *Boswellia serrata*, German chamomile, dandelion or feverfew.

Group B vitamins

Group B vitamins are very important because they are cofactors in many enzymatic reactions related to cell metabolism. Their deficiency can be very harmful to health.

Two of these vitamins, **B12 or cobalamin** and **B9 or folic acid**, as they are ingested in the diet or as they are in most supplements, are not active and need to be methylated in the liver to be transformed into the active form.

The methylation process is complex, and **genetic polymorphisms** have been found in two of the most important enzymes, COMT and MTHFR, which produce enzymes with lower activity. In these cases it will be necessary to increase the usual doses or, better, to recommend supplements of the already methylated vitamins.

Gene	Rs identifier	Polymorphism	Results
COMT	rs4680	Val158Met	Val/Met
MTHFR	rs1801133	677C>T	GA

Consequences

The detected genotype for **COMT** gene is associated with a normal enzymatic activity.

The detected genotype for **MTHFR** gene is associated with slightly slow enzymatic activity and slightly increased homocysteine levels, which may result in increased susceptibility to cardiovascular damage.

Recommendations

• **Increase** intake of **methylated group B vitamins** (especially vitamins B6, B9, B12) as well as **betaine** and **choline** either through diet and/or with nutritional supplements.

• **Limit coffee** consumption to a maximum of 3 cups per day to avoid increasing cardiovascular risk.

Vitamin D

Vitamin D, also called calciferol, is an essential fat-soluble vitamin. It can be obtained in three ways:

- By **exposing** the skin cells to the sun's rays (UV). However, when wearing clothes and using sunscreens the synthesis by the action of the sun's rays is very low.
- By eating Vitamin D**rich food**, such as sardines, tuna, mackerel and salmon, as well as milk and eggs.
- Nutritional **supplements**, the most common way to maintain adequate levels.

Vitamin D deficiency is related to many pathologies among which **osteoporosis**, **hypocalcemia** and **osteomalacia** stand out.

The action of vitamin D may be influenced by polymorphisms in several genes: **CYP2R1** (Cytochrome P2R1) responsible for synthesizing active vitamin D, **VDBP** (Vitamin D Binding Protein) to which it is binded for transport, and **VDR** (Vitamin D Receptor) responsible to codfy its receptor in the tissues.

Gene	Rs identifier	Polymorphism	Results
CYP2R1	rs10741657	-1127T>C	AG
VDBP	rs7041	1296 T>G	AA
VDR	rs1544410	BsmI	CT

Consequences

The detected genotype for **CYP2R1** is associated with a slightly reduced levels of endogenous synthesis of active vitamin D, which may increase the risk of vitamin D deficiency.

The detected genotype for **VDBP** is related to higher affinity of the binding protein for vitamin D, which will result in a lower than expected levels of free vitamin D, which may increase the risk of a functional vitamin D deficit.

The detected genotype for **VDR** is related to a slightly reduce affinity of the receptor for vitamin D, which results in a decrease vitamin D efficiency.

Recommendations

Recommendations

• **Ensure** adequate **vitamin D** intake. If it is difficult to obtain it through the diet, an additional intake through nutritional supplements is suggested.

• **Consume** foods rich in **vitamin D3**.

• **Prefer calcium-rich products** to optimize bone mineralization.

• **Limit** consumption of products rich in **phosphorus** to a maximum of 700 mg per day. Also **avoid** foods bearing the code **E 338-452**, under which phosphates are hidden on food labels.

• **Consume** foods rich in **flavonoids** (present in tea, garlic, onions, blueberries, grapes...).

• **Practice** regular **physical activity**.

• Unless there are other risk factors that contraindicate it, it is good to **expose yourself to sunlight** without protection for about 10-15 minutes a day, on a regular basis and with the maximum number of cells exposed to the sun. Afterwards, apply sunscreen and avoid excessive sun exposure in the middle of the day.

Hunger – satiety control

Leptin is an **anorectic** hormone related to weight control through the control of feelings of hunger and satiety. In the **hypothalamic arcuato nucleus** the **neuropeptide NPY** is produced which increases the sensation of hunger. **Leptin inhibits the secretion of NPY**, a mechanism that acts as an **appetite suppressant**. It is secreted by the fat cells in states of high energy availability, preventing the sensation of hunger from being activated.
In **obese** people, abundant leptin is secreted, which can lead to **resistance or insensitivity to the hormone**, and therefore favour food intake, due to imbalance in the effects of leptin. The genetic variant analyzed is associated with increased leptin levels.

Ghrelin is a hormone with different functions, the best known being the **control of the balance between hunger and satiety.** The intestine secretes ghrelin in a fasted state, which has an **orexygen** effect on the central nervous system, which is why it has been nicknamed **"hunger hormone"**. Have also effect on insulin secretion and on glycogenolysis and glycogenesis. The variant Genetics being analyzed are associated with lower ghrelin production.

Beta-adrenergic receptors have multiple functions. In terms of weight control, they are related to the **mobilization of energy reserves,** mainly stored in fats, through the **stimulation** by **catecholamines** (adrenaline and noradrenaline). The analyzed genetic variant is associated with less stimulation of the beta 2 receptor and consequently less fat mobilization.

Gene	Rs identifier	Polymorphism	Results
ADRB2	rs1042713	Arg16Gly	AA
GHRL	rs696217	Leu72Met	GG
LEP	rs13245201	1414G>A	AG

Consequences

The detected genotype for **LEP** gen is associated with increased leptin levels.

Recommendations

• **Increase fiber** intake. Consumption of foods rich in **soluble fiber** for its ability to increase satiety.

• **Prefer** a diet rich in **monounsaturated** (olive oil, olives ...) and **polyunsaturated** (fish, legumes, seeds, nuts ...) fatty acids which protect against an increase in waist circumference and can lead to a reduction in BMI.

• **Avoid strict diets** and the **"yo-yo" effect** since the rapid loss of weight consists essentially of water and muscle mass, and is usually regained as soon as the diet is interrupted. It is important to lose fat and modify the body composition to increase the basal metabolism.

• **Regular physical activity** contributes to blood glucose control by improving insulin sensitivity, through reducing body weight and increasing insulin binding capacity.

Lactose intolerance

Lactose is the sugar in milk. It is a **disaccharide** composed of **glucose** and **galactose**. The **enzyme lactase** cleaves lactose into the two monosaccharides which are absorbed in the intestine. The lactase activity depends on the LCT gene. In mammals, as they do not drink milk in adulthood, the gene reduces its expression and eventually stops synthesizing lactose.

When man started to take milk regularly in the adulthood, there has been an **adaptive mutation** of the LCT gene, which causes it not to be deprogrammed. In Spain, 20% of the population continues having two ancestor alleles, therefore becoming lactose intolerant. Intolerance usually manifests itself in childhood, but can also appear in adults who can spend years with digestive disorders without being related to a genetic intolerance lactose. It is therefore of interest to perform the genetic test.

Gene	Rs identifier	Polymorphism	Results
LCT	rs4988235	-13910C>T	CC

Consequences

The detected genotype for **LCT** gene is associated with the presence of lactose intolerance. This genotype leads to a decrease or cessation of lactase expression in adulthood.

This test only refers to primary lactose intolerance. It does not exclude other pathologies such as secondary intolerance, intestinal dysbiosis or of an immunological nature.

Recommendations

The lactose intolerance can be of a **very variable magnitude**. The degree of intolerance can be **mild** and **not lead to discomfort** with a normal consumption of lactose, however it must be borne in mind that the deficiency can be made patent with a higher consumption of lactose, and this can **increase with age**, eventually manifesting a **full intolerance**.

Therefore, in spite of not presenting symptomatology, it is recommended to:

- **Avoid dairy products** (especially milk and cheese) in the diet.
- If in doubt whether there is lactose in the food, **supplement** with **lactase enzyme**.

Celiac disease

Celiac disease is an autoimmune inflammatory disease that affects between 1 and 2% of the population. It is caused by an abnormal activation of the lymphocytes in the membranes of the small intestine, which is triggered by the gluten protein (gliadin) and occurs in people who are positive for the genetic markers **HLA-DQ2 or HLA-DQ8**.

Having a negative result for both markers excludes, with a 98% probability, a coeliac condition; 70% of non-celiacs can be excluded in this way. 30% of the population has one or two positive markers, in homozygosis or heterozygosis and **such positivity is necessary, but not sufficient**, for a diagnosis of coeliac disease. The definitive diagnosis must be made by a specialist, taking into account, in addition to genetic positivity, the patient's clinic, other laboratory tests and in some cases an intestinal biopsy.

There is also the so-called "intolerance or sensitivity to gluten", which requires other tests and is more heterogeneous and difficult to diagnose.

Gene	Rs identifier	Polymorphism	Results
6p21 (DQ2.5)	rs2187668	C>T	CC
6p21 (DQ8)	rs7454108	T>C	TT

Consequences

The results obtained **exclude** the **possibility** of current or future **gluten intolerance** with high, although not absolute, reliability. Approximately 95% of gluten-intolerant individuals carry one of the DQ2.5 or DQ8 risk alleles, but in a small proportion of cases this is due to other factors not analyzed in this study.

Recommendations

• In **asymptomatic people** this results excludes a risk of developing celiac disease with high reliability, and therefore there is **no medical reason** to **remove gluten** from the diet.

• In case of celiac-like **symptoms**, a **differential diagnosis** with other compatible disease, such as dyspepsia, inflammatory bowel syndrome or inflammatory bowel disease should be considered.

Hereditary hemochromatosis

It is a **hereditary disease** that affects 1 in 200 people. It causes an excessive **accumulation** of **iron** in the **organs** and **systems** of the body.

It is caused by various **mutations in the HFE** gene, 87% of cases being caused by the Cys282Tyr and His63Asp mutations. For the disease to **manifest** itself, a **single mutation is not enough**. Only some people with the genotype of hemochromatosis end up **manifesting clinical symptoms**. Moreover, it usually appears from the fourth decade of life, when the **deposit of iron** already causes **damage to the organs** where it accumulates (especially the liver and lungs).

For this reason it is **interesting to detect** it, in order to, if positive, initiate **preventive measures** that avoid as soon as possible the progressive injury of the affected organs.

It should be taken into account that **other pathologies**, both genetic and non-genetic, can be treated with iron overload and have a similar symptomatology to hereditary hemochromatosis.

Gene	Rs identifier	Polymorphism	Results
HFE	rs1800562	Cys282Tyr	GG
HFE	rs1800730	Ser65Cys	AA
HFE	rs1799945	His63Asp	CC

Consequences

None of the **HFE-associated hereditary hemochromatosis mutations** have been detected. However it can not be excluded with absolute certainty because there may be other rare mutations that are not analyzed in this study.

Recommendations

If there is a **biochemical or clinical presentation** compatible with hemochromatosis, you should consider a **differential diagnosis** to evaluate other genetic and non-genetic iron overload disorders.

Inflammation mediators

Interleukins (IL) and **tumor necrosis factor (TNF)** are a collection of molecules called **cytokines** that have the function of establishing communication between cells. They are released by the **immune system**. They are proteins (therefore their activity may depend on polymorphisms in the genes that encode them) and their function in the body is to coordinate the response of the immune system and they do this by stimulating or inhibiting the **functions of cells**, regulating the **proliferation and cell differentiation**, and **activating or inhibiting the expression of some genes**. They mediate many of the functions of the cells responsible for **innate and acquired immunity**. They are involved in the development and activation of immune system cells and the inflammatory response.

IL secretion has a great importance in stress. In the early stages of stress, there is a positive reaction, increasing the secretion of **anti-inflammatory IL**. But when stress is prolonged, **proinflammatory IL** synthesis increases, contributing to the detrimental **effects of prolonged stress.**

In some ILs are known **polymorphisms** in the gene that encodes them, which affect their level of expression, so that, when faced with the **same level of stimulus**, people can synthesize **more or less of a certain IL**, depending on their genotype. It is therefore interesting to know the genotype-phenotype of these variants, as the risk may be customized to be more or less susceptible to inflammatory processes.

Gene	Rs identifier	Polymorphism	Results
IL10	rs1800896	-1082G>A	TT
IL1A	rs1800587	-889G>A	AG
IL1B	rs1143634	315C>T	GA
IL6	rs1800795	-174C>G	GG
TNFa	rs1800629	-308G>A	AG

Consequences

The detected genotype in the studied genes, considered globally, supposes a much **higher risk of inflammation** compared to the majority of the population.

Recommendations

Due to the **highly pro-inflammatory genotype**, it is recommended to follow the following recommendations more **rigorously and strictly**:

• **Avoid** being **overweight** and **obesity**, since they directly influence on low-grade inflammation.

• **Include omega-3 fatty acids** (fish oil, krill, and/or chia or flax seeds) and/or consider supplementation.

• **Avoid** foods rich in **trans fatty acids** present in ultra-processed foods, foods rich in **saturated fatty acids** and **omega-6 with arachidonic acid**, especially mammalian meat, also poultry and dairy products and, to a lesser extent, eggs.

• **Reduce oxidative stress** by increasing the intake of **fruits** (citrus, red fruits ...) and **vegetables** (cruciferous, garlic, onion) **rich in antioxidants** (vitamin C, vitamins A and E, zinc, selenium, quercetin ...).

• **Reduce simple sugars** (white, cane or brown sugar) as they are highly inflammatory and acidifying.

• Consume **green tea** that is rich in **flavonoids** and anti-inflammatory **catechins.**

• Incorporate **spices** such as **turmeric,** rich in curcumin, **ginger, oregano, basil,** thyme, peppers or stevia into the diet.

• **Red grapes** and **red wine** are a source of **resveratrol,** which is a powerful antioxidant.

• Consume foods rich in **L-arginine** in oily fish (such as bonito, horse mackerel and mackerel), walnuts and grapes. In the case of a deficient diet, it is recommended to supplements.

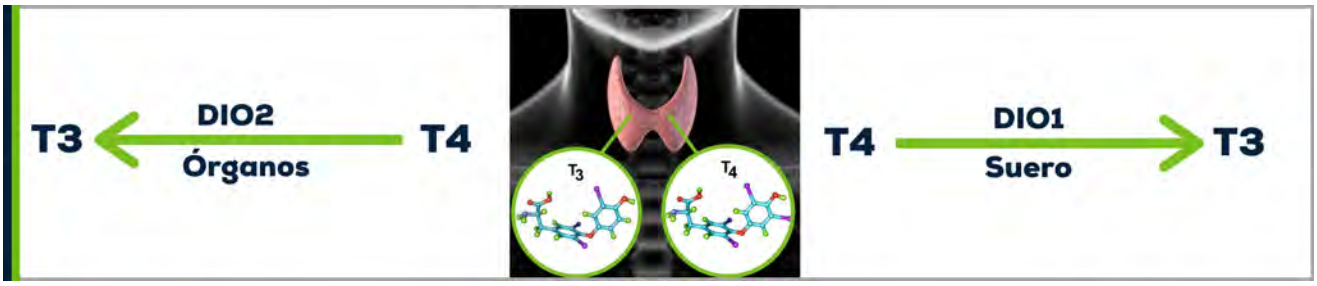
• **Avoid** excessive **alcohol** consumption.

• **Reduce stress** and get a minimum of 8 quality hours of sleep, as well as, **perform moderate exercise** on a regular basis.

• **Treat** any **digestive problems** and any process that causes alteration of intestinal and mucous permeability (dysbiosis, irritable bowel, ulcerative colitis, celiac disease ...).

• In acute inflammation, consult your doctor or pharmacist about the option of prescribing **supplementation** with products that reduce inflammation such as: **willow**, **devil's claw**, **boswellia**, **arnica** ... among others.

Clinical hypothyroidism with normal serum T3 levels



The main circulating **thyroid hormone** is **T4** (thyroxine or tetra-iodothyronine), which is the main one produced by the thyroid. However, the **most active hormone** is **T3** (triiodothyronine) and consequently, the metabolic response to the hormone will be dependent on the formation of T3.

The **DIO2 gene** encodes the enzyme DIO2 which converts T4 into T3 in brain, muscle and fat tissues, and the **DIO1 gene**, encodes the enzyme DIO1, which does so in peripheral circulation. No relevant polymorphisms are known for the DIO1 gene, but the **DIO2** gene has a **missense mutation**, rs225014 T>C, which causes the substitution of a threonine by an alanine in the amino acid chain of the DIO2 enzyme at position 92 (Thr92Ala). This change in the active center of the enzyme alters its binding to the selenium-cysteine cofactor and results in **less activity** and therefore **less T3 formation in organs**. In other words, a functional hypothyroidism with normal serum levels of T3.

The heterozygous form (CT) and especially the homozygous variant (CC) have been associated with obesity, insulin resistance, problems in the adjustment of glycemia, osteoarthritis and cognitive problems.

Gene	Rs identifier	Polymorphism	Results
DIO2	rs225014	Thr92Ala	CT

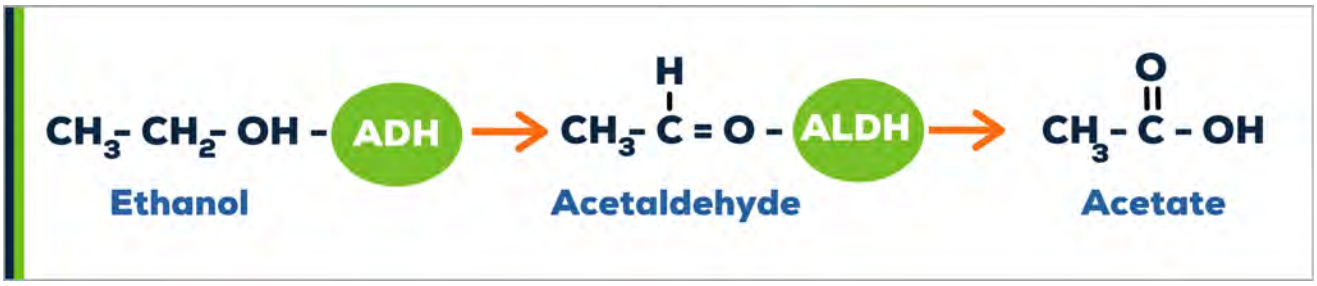
Consequences

The detected genotype for the **DIO2** gene is related to a partially decreased tissue conversion from T4 (thyroxine) to T3 (triiodothyronine) although there may be normal serum levels of both hormones.

Recommendations

The heterozygous state *per se* may not lead to clinical signs. However, it may do so in conjunction with other factors. Therefore, it must be taken into account if the patient presents **clinical symptoms of a slight hypothyroidism**, such as fatigue, increased sensitivity to cold, constipation, dry skin, weight gain, swelling of the face, hoarseness, muscle weakness, among others. In that case it is advisable to supplement with lyothyronine or triiodothyronine.
The control of the response must be clinical, since the serum values, in the absence of other thyroid pathology, will be normal.

Alcohol metabolism



Alcohol is metabolized mainly in the **liver**. By the enzyme **alcohol dehydrogenase** (ADH) it is transformed into **acetaldehyde**, and this, thanks to the enzyme **aldehyde dehydrogenase** (ALDH) is transformed into **acetate**.

There are **genetic variants** in these enzymes (ADH and ALDH) that **modulates their activity** and facilitate in the short term the appearance of symptoms such as skin flushing, nausea and headache. Also, in the long term, exposure to acetaldehyde facilitates the development of liver pathologies linked to alcohol consumption. It has been reported that **higher ADH activity** and **lower ALDH activity** may confer risk in some population for the **accumulation of acetaldehyde**, which is toxic for the body.

In addition to genetic factors, **age** and **gender** may **affect** the **alcohol metabolism.**

Gene	Rs identifier	Polymorphism	Results
ADH1B	rs1229984	His48Arg	CC
ALDH2	rs671	42076G>A	GG

Consequences

The genotypes detected are related to normal enzyme activity, leading to **normal alcohol metabolism**, being the most frequent in the general population.

Selection of revised bibliography

To create this report, we have been reviewed contrasted scientific publications, are available upon request. A selection of the most relevant ones is shown below.

• Abbas S, Nieters A, Linseisen J, et al. Vitamin D receptor gene polymorphisms and haplotypes and postmenopausal breast cancer risk. Breast Cancer Res. 2008;10(2):R31. doi: 10.1186/bcr1994.

• Adams P, Altes A, Brissot P, et al. Therapeutic recommendations in HFE hemochromatosis for p.Cys282Tyr (C282Y/C282Y) homozygous genotype. Hepatol Int. 2018 Mar;12(2):83-86. doi: 10.1007/s12072-018-9855-0.

• Bikle DD. Extraskeletal actions of vitamin D. Ann N Y Acad Sci. 2016 Jul;1376(1):29-52. doi: 10.1111/nyas.13219.

• Gomez P, Perez-Martinez P, Marin C, et al. APOA1 and APOA4 gene polymorphisms influence the effects of dietary fat on LDL particle size and oxidation in healthy young adults. J Nutr. 2010 Apr;140(4):773-8. doi: 10.3945/jn.109.115964.

• Gouda HN, Sagoo GS, Harding AH, et al. The association between the peroxisome proliferator-activated receptor-gamma2 (PPARG2) Pro12Ala gene variant and type 2 diabetes mellitus: a HuGE review and meta-analysis. Am J Epidemiol. 2010 Mar 15;171(6):645-55. doi: 10.1093/aje/kwp450.

• Mattar R, de Campos Mazo DF, Carrilho FJ. Lactose intolerance: diagnosis, genetic, and clinical factors. Clin Exp Gastroenterol. 2012;5:113-21. doi: 10.2147/CEG.S32368.

• Ng ZY, Veerapen MK, Hon WM, Lim RL. Association of leptin/receptor and TNF- gene variants with adolescent obesity in Malaysia. Pediatr Int. 2014 Oct;56(5):689-97. doi: 10.1111/ped.12336.

• Poon AH, Gong L, Brasch-Andersen C, et al. Very important pharmacogene summary for VDR. Pharmacogenet Genomics. 2012 Oct;22(10):758-63. doi: 10.1097/FPC.0b013e328354455c.

• Rogers PJ, Hohoff C, Heatherley SV, et al. Association of the anxiogenic and alerting effects of caffeine with ADORA2A and ADORA1 polymorphisms and habitual level of caffeine consumption. Neuropsychopharmacology. 2010 Aug;35(9):1973-83. doi: 10.1038/npp.2010.71.

• Sánchez-Moreno C, Ordovás JM, Smith CE, et al. APOA5 gene variation interacts with dietary fat intake to modulate obesity and circulating triglycerides in a Mediterranean population. J Nutr. 2011 Mar;141(3):380-5. doi: 10.3945/jn.110.130344.

• Thorn CF, Aklillu E, McDonagh EM, et al. PharmGKB summary: caffeine pathway. Pharmacogenet Genomics. 2012 May;22(5):389-95. doi: 10.1097/FPC.0b013e3283505d5e.

• Tsilidis KK, Helzlsouer KJ, Smith MW, et al. Association of common polymorphisms in IL10, and in other genes related to inflammatory response and obesity with colorectal cancer. Cancer Causes Control. 2009 Nov;20(9):1739-51. doi: 10.1007/s10552-009-9427-7.

Additional information

The genetic polymorphisms included in this report have been selected on the basis of scientific publications that endorse their interpretative value for predicting individual health risks.

There are changes in genes, which do not directly cause disease, but which alter the activity of an enzyme, a transport protein or a receptor, which may themselves condition metabolic dysfunction, or in association with other variants. Therefore, they can predispose to diseases or health alterations, if life habits are not implemented and if appropriate nutritional or pharmacological supplements are not used.

Its objective is to make a risk prediction, i.e. Predictive Medicine, in order to implement a Personalized Preventive Medicine.

The genetic polymorphisms that appear in this report are not directly a specific diagnosis, but a complementary help for the health professional who has requested them. Consequently, it is solely responsible for the conclusions and recommendations to the patient that it deems appropriate in each case, regardless of what can be stated in general terms in this report.

It is the responsibility of the health care professional to incorporate the data in this report and any recommendations that may arise from the interpretation of these polymorphisms into the patient's medical record, along with other results from conventional analyses or other complementary explorations.

This report may contain lists of suggested foods based on their nutrient content that may be beneficial to the patient. However, such foods may not be indicated for food intolerances, allergies, specific diets, or medications that the patient may be taking. Therefore, this report and its contents should be reviewed together with the prescribing physician and decide within the suggested foods which to take. If not, establish other food supplements.

The processing laboratory is responsible for the accuracy of the results obtained, but the interpretation of the results is the responsibility of the health professional who requested them.

The genetic results presented do not allow us to conclude with certainty about the development of a disease or its susceptibility, because the tests carried out do not allow us to consider all the factors that contribute to the relative risk of a given susceptibility or of the possible evolution of a disease. Complex variables such as the degree of risk to develop adverse effects to drugs, or to suffer from multifactorial diseases in which genetic factors are not totally determinant are also relevant.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