DENTALgenes

Dental health profile

Surname: Ejemplo		**Reception date:** -	
Name: Paciente		**Validation date:** -	
Birth Date: -		**Sample Type:** -	
ID nr: -	**Gender:** -	**Physician:** -	
Order: -		**Validation by:** -	

Objective of this profile

The aim is to evaluate personal **predisposition**, based on the study of genetic polymorphisms, to suffer problems related to **dental health**. The purpose is that the stomatologist can plan **personalized** preventive examinations and, if necessary, corrective measures according to the need and risk of each person.

Caries

Caries are permanent structural damage on the surface of the teeth that become small openings or holes. Their development depends on diet, saliva composition and tooth enamel.

Composition of saliva
It is important to maintain an adequate pH and buffering capacity of saliva, as they influence the nature of the microbiota. Some polymorphisms can alter the composition of saliva and consequently the risk of caries.

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Amelogenesis
It is the process of enamel formation in teeth. Certain genetic polymorphisms can affect both the formation and structure of enamel, contributing to alterations that could favor mineral loss and/or bacterial adhesion.

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Sugar consumption
Sugar consumption is one of the main factors in cariogenesis. There are polymorphisms that are related to the preference and/or intake of sweets and to an increased risk of caries.

Bruxism

Known as teeth grinding, it is a pathology characterized by an involuntary contraction of the jaw muscles producing wear on the teeth. Certain polymorphisms are associated with a greater or lesser risk of bruxism.

Periodontitis

It is an inflammatory disease of the gums that damages the soft tissue and can destroy the bone that supports the teeth, causing them to loosen or even fall out. This disease is linked to inflammatory processes and can be favored by polymorphisms that affect the secretion of interleukins, among others.

Periodontitis and other pathologies

Periodontitis, being an inflammatory pathology and promoting the synthesis of interleukins, has been associated with increased risk of cardiovascular disease, rheumatoid arthritis and diabetes.

Selected genetic polymorphisms

The genetic variants analyzed for this report are shown below. Based on the results obtained, nutritional and lifestyle recommendations adapted to your profile are provided. Additional information on these recommendations can be found in the Supplementary Information section. It is essential that, before taking any **nutritional supplement** together with **medication**, you **consult** your **doctor** to avoid **adverse reactions** to medications.

The risk assessment was carried out by implementing **statistical models** based on **103 scientific publications**. Specifically, data from 53 meta-analyses involving more than 60,000 individuals were used to calculate the risk of periodontitis.

Gene	Rs Number	SNP	Results
ACTN3	rs1815739	p.Arg577Ter	TT
AMBN	rs7439186	764C›T	CT
AMELX	rs17878486	55-951T›C	CC
AQP5	rs3759129	4159A›C	CC
AQP5	rs10875989	797T›C	TC
CA6	rs17032907	259+904C›T	TT
CA6	rs2274326	80-108C›T	CC
COMT	rs6269	1-98A›G	AG
DRD2	rs6277	957C›T	GA
DRD2	rs6275	939A›G	AA
DRD2 (ANKK1)	rs1800497	32806C›T	AA
DRD3	rs6280	25C›T	TT
ENAM	rs3796704	2288G›A	GA
HTR2A	rs6313	102G›A	AA
IL10	rs1800896	-1082G›A	CT
IL10	rs1800872	-592T›G	TG
IL18	rs187238	-137C›G	CC
IL1A	rs1800587	-889G›A	AG
IL1B	rs1143634	315C›T	GG
IL6	rs1800796	85+369G›C	GC
IL6	rs1800795	-174C›G	CC
KLK4	rs2235091	613-129A›G	AG
KRT75	rs2232387	481C›T	CC
LTF	rs13070740	44-1905G›A	GG

Gene	Rs Number	SNP	Results
MMP9	rs3918242	-1562G›A	GG
SLC2A4	rs5415	4428T›C	TT
TAS1R2	rs35874116	571T›C	TC
TAS1R3 (INTS11)	rs3845293	-32+26A›C	AC
TAS2R38	rs1726866	785G›A	GG
TNFa	rs1800629	-308G›A	AG
TUFT1	rs3790506	415-273G›A	GA
TUFT1 (CGN)	rs7552458	14-2200T›G	GG
VDR	rs731236	Taql	AA

Risk genotype	Normal genotype	Protective genotype

Caries - Composition of saliva

Saliva directly **affects** the **three etiologic components of caries** (tooth, plaque and substrate). It affects pathogen flow and clearance rates, **maintaining pH** and buffering capacity, calcium phosphate homeostasis and **effects on bacterial metabolism**. It can increase the adsorption of pathogens to oral tissues or remove them from the oral cavity.

Aquaporin 5 (AQP5) plays a **fundamental role in the production of saliva**, tears and pulmonary secretions, regulating the amount of water they contain. **Proper hydration** of saliva makes it difficult for microorganisms to adhere to the dental film.

Carbonic anhydrase isoenzyme VI (CA6) is expressed exclusively in the parotid and submandibular glands and plays a key role in the oral microenvironment, influencing the **pH buffering capacity** of saliva.

Finally, **lactotransferrin** (LTF) is an iron-binding glycoprotein found in milk and body secretions, including saliva, and exhibits **potent antibacterial** and immune-activating activity.

Gene	Rs Number	SNP	Results
AQP5	rs3759129	4159A›C	CC
AQP5	rs10875989	797T›C	TC
CA6	rs17032907	259+904C›T	TT
CA6	rs2274326	80-108C›T	CC
LTF	rs13070740	44-1905G›A	GG

Consequences

The genotype detected in the **AQP5** gene confers an increased risk of caries. This genotype is associated with lower levels of water in saliva and with a worse ratio of aggregation and elimination of microorganisms, compared to carriers of the reference allele in the two variants.

The genotype detected in the **CA6** gene confers an increased risk of caries. This genotype is associated with a worse saliva pH buffering capacity and a higher caries risk compared to carriers of the reference allele in both variants.

The genotype detected in the **LTF** gene, despite being the most frequent in the population, is related to an increased risk of caries with respect to the heterozygote. This genotype has been associated with lower levels of lactoferrin, which translates into a lower capacity to inhibit *S. mutans* and therefore, a higher risk of caries.

Recommendations

• **Reduce stress** and **anxiety** levels, since they alter the production of saliva reducing it.

• **Use** appropriate **mouthwashes** to treat **xerostomia**.

• **Consider substitution** or **reduction** of **xerostomizing drugs** such as tricyclic antidepressants, antiparkinsonians, benzodiazepines, some antihypertensives, antihistamines and diuretics.

• **Use sialogogues** to promote saliva secretion.

• **Use salivary substitutes and/or wetting agents** such as Betaine, Xylitol, Allantoin, Aloe vera and Sodium Fluoride as part of daily oral hygiene.

• **Drinking** larger amounts of **water** to keep the mouth well hydrated.

• It is advisable to **consume specifically neutral pH water**.

• **Avoid highly acidifying foods** such as refined sugar, meats, seafood, cheeses, whole eggs, refined salt, corn, flour, white bread, packaged foods, chocolate, beer, tea, coffee.

• If consumed, balance them with a **varied diet rich in more alkaline vegetables** such as pumpkin, beets, celery, lettuce, zucchini, garlic, onion, parsley, raw spinach, broccoli and cabbage.

• **Avoid** soft drinks, carbonated beverages rich in **phosphoric acid** and **alcohol**.

• It is important to **improve the cleaning technique** and use **dental floss** to remove food debris and prevent the accumulation of dental tartar.

• It is best to use **fluoride toothpaste**.

• It is **recommended** to **eat raw, bitten and unpeeled fruit** (especially strawberries, apples and melon). Other recommended foods are parsley and sesame seeds.

• **Increase visits** to the **dentist** to control inflammation and bleeding gums, gingivitis or periodontitis. If necessary, scaling and root planing is recommended.

• **Smoking** can also cause an increased accumulation of **oral bacteria**.

• To evaluate these **bacteria**, an **oral dysbiosis** test is recommended.

• **Lactoferrin supplements** may be recommended.

Caries – Formation and structure of the enamel

The **structural proteins of the enamel matrix** determine the growth and **development of hydroxyapatite crystals**, the mineral that forms dental enamel. The most important proteins of the enamel matrix structure are: amelogenin, ameloblastin, enamelin, tuftelin, kallikrein 4 and keratin 75. Polymorphisms have been described in the genes that encode them that alter their structure and therefore can increase the risk of caries. The genes are respectively: **AMELX**, **AMBN**, **ENAM**, **TUFT1**, **KLK4** and **KRT75**. All except KRT75 are also associated with hereditary diseases of dental development such as dentinogenesis imperfecta or amelogenesis imperfecta.

Although the final structures produced are very different and involve specific structural components, the formation of **teeth** and **hair** use some common molecular pathways. In hair, hair keratins form highly cross-linked filaments and form the different layers of the hair shaft and supporting tissues. In the tooth, keratins have also been shown to provide a complex structure upon which enamel is formed.

Finally, variations in all these genes can **affect the structure** during the enamel mineralization process, contributing to alterations that could favor **mineral loss** and/or **bacterial adhesion**. **Weaker** and more **porous** enamel is in turn **less resistant** to dental caries.

Gene	Rs Number	SNP	Results
AMBN	rs7439186	764C›T	CT
AMELX	rs17878486	55-951T›C	CC
ENAM	rs3796704	2288G›A	GA
KLK4	rs2235091	613-129A›G	AG
KRT75	rs2232387	481C›T	CC
TUFT1	rs3790506	415-273G›A	GA
TUFT1 (CGN)	rs7552458	14-2200T›G	GG

Consequences

The genotype detected in the genes studied in relation to enamel, considered globally, is associated with a higher risk of caries compared to the majority of the population.

Recommendations

• The most effective **preventive solution** is to brush your teeth after every meal and try not to snack between meals.

• It is important to **improve the cleaning technique** and use **dental floss** to remove food debris and prevent the accumulation of dental tartar.

• It is best to use **fluoride toothpastes**.

• Avoid consumption of **abrasive foods** such as carbonated or alcoholic beverages, acidic and spicy foods.

• Smoking can also cause an increased accumulation of oral bacteria.

• **Keratin supplements** may be recommended.

Caries - Sugar consumption

Sugar consumption is a risk factor in **cariogenesis**. The consumption of simple carbohydrates is modulated by **sociocultural** and **physiological factors**, mainly the **preference for sweet taste**. It involves everything from glucose transporters to neuronal receptors.

On the one hand, some **glucose transporter proteins** are associated with the consumption of sugar derivatives. Among them, **SLC2A4**, which is involved in the transport of glucose from blood to saliva.

On the other hand, taste receptors directly affect the perception of flavors. **TAS1R2** and **TAS1R3** receptors are responsible for **sensitization to sweetness**. **TAS2R38** is a receptor that **controls bitter taste** and is also related to hypersensitivity to sweetness.

There are polymorphisms in all these genes that modulate the ability to **detect sweetness**, so that some people need larger amounts of sugar to notice it.

Finally, another factor affecting eating habits stands out: the **neuronal response to food**. Tasty foods (especially sweets) trigger a dopamine-mediated response in the **reward system**. The **DRD2** receptor modulates it and polymorphisms in its gene are associated with a more intense reward response, which may lead to a tendency to **overeat**.
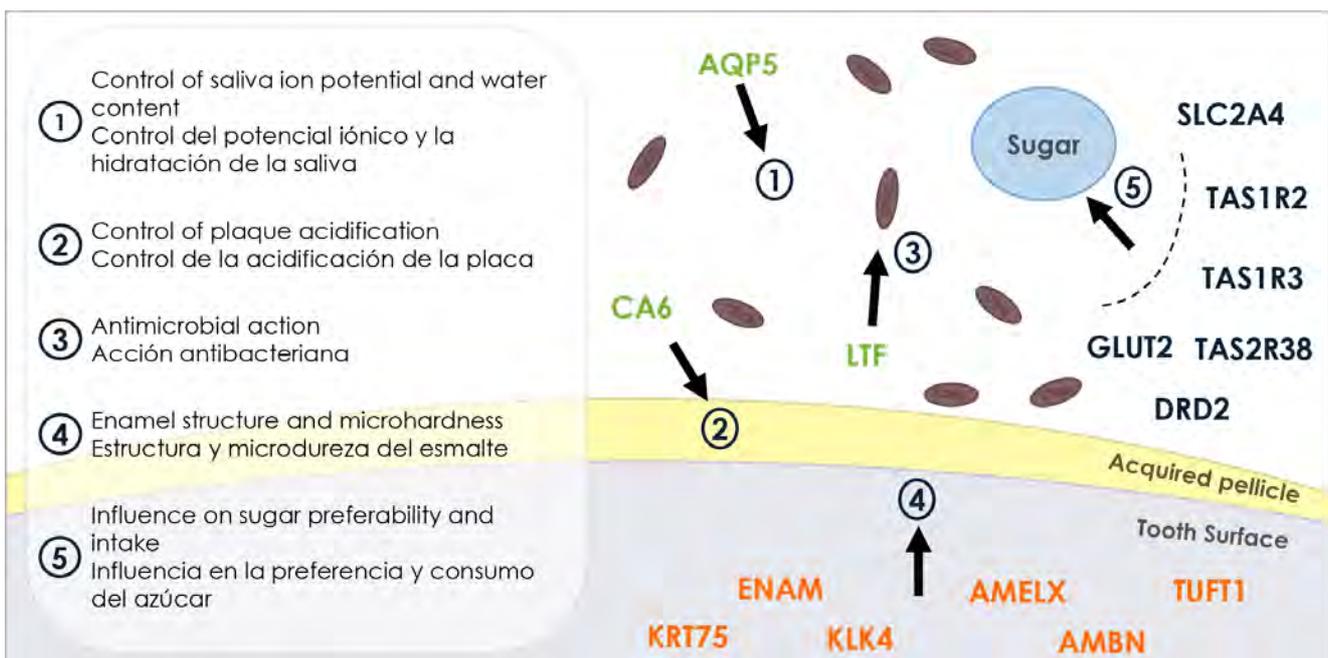
Gene	Rs Number	SNP	Results
DRD2	rs6277	957C›T	GA
SLC2A4	rs5415	4428T›C	TT
TAS1R2	rs35874116	571T›C	TC
TAS1R3 (INTS11)	rs3845293	-32+26A›C	AC
TAS2R38	rs1726866	785G›A	GG

Consequences

The detected genotype in the studied genes, considered globally, is associated with a preference for sweets and a consumption of sugar that corresponds to the majority of the population.

Recommendations

The genotype detected is related to a **normal appetite for sugars**. However, in a **context** such as the **current** one where the majority of the **population consumes a large amount of sugars**, it is very important to follow a **healthy lifestyle low in simple sugars** to reduce the risk of caries. To this end, it is recommended to:

• **Reduce simple sugars** such as white, cane or brown sugar, fructose, honey, jams, sugary drinks etc. and replace it with **fruits** or sweet spices such as **cinnamon**, **vanilla** or **pure cocoa**.

• **Replace** "**white**" cereals with **whole-grain** carbohydrates.

• Preferably choose **low glycemic index fruits**.

• **Replace** sugar with **healthy sweeteners** such as stevia, unsweetened applesauce or **fresh** or **dried fruit**.

• **Pay attention to labels** and watch the nutritional information on foods.

Bruxism

Bruxism, commonly known as **teeth grinding**, can occur during the day or, more frequently, at night and is suffered by approximately **50% of the population** in Spain. It occurs due to **involuntary contractions** of the masseter, temporal and other jaw muscles, which wear down the enamel.

Neurotransmitters and receptors and enzymes of the **serotonergic and dopaminergic pathways** are responsible for the circadian cycle, maintain arousal, regulate stress response and motor control, among many other functions. Of particular interest in bruxism are the serotonin receptor 2A (**HTR2A**) and the dopamine D2 and D3 receptors (**DRD2** and **DRD3**). Similarly, **ANKK1** encodes a protein involved in cellular signal transduction and its gene is closely related to the DRD2 gene. In addition, catechol-O-methyltransferase (**COMT**) is an enzyme that catalyzes the first link - demethylation - in the metabolism of catecholamines, such as dopamine and adrenaline, and is also fundamental in the regulation of these neurotransmitters at the synapse.

Polymorphisms have been described in the genes encoding these proteins, and their effects are associated with **behavioral or emotional alterations** (stress and anxiety, for example) and even with some dyskinesias, involuntary movement disorders.

Finally, actinin alpha 3 protein (**ACTN3**) is expressed only in fast muscle fibers and is involved in the function of some muscles, such as the jaw muscles.
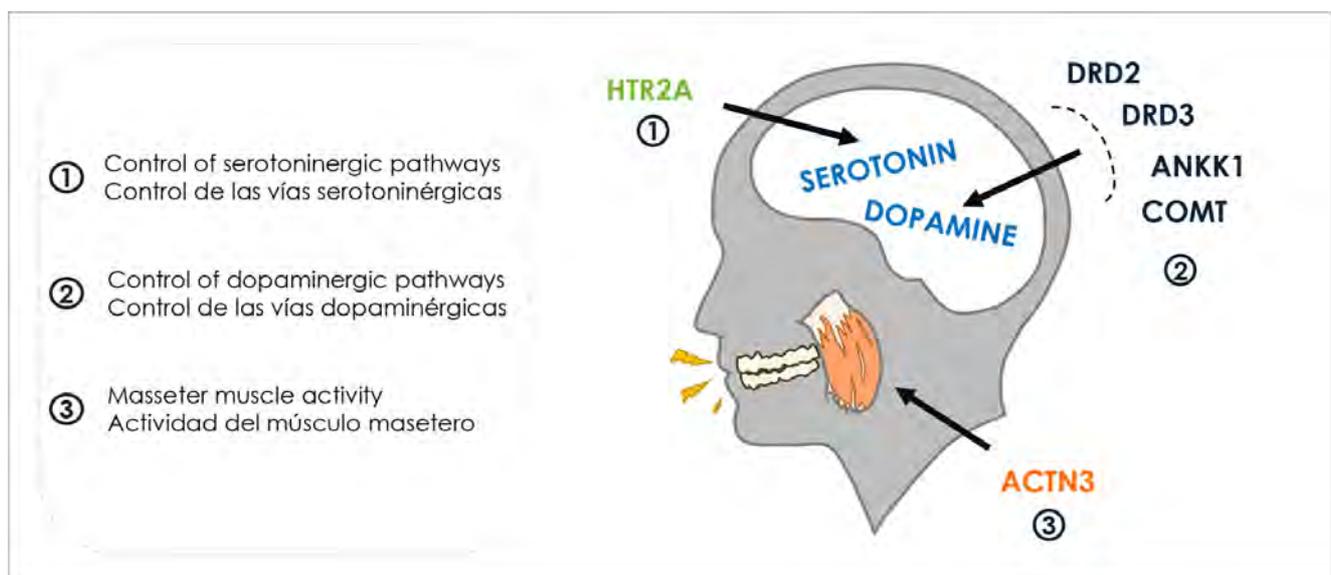
| Gene	Rs Number	SNP	Results
ACTN3	rs1815739	p.Arg577Ter	TT
COMT	rs6269	1-98A›G	AG
DRD2	rs6275	939A›G	AA
DRD2 (ANKK1)	rs1800497	32806C›T	AA
DRD3	rs6280	25C›T	TT
HTR2A	rs6313	102G›A	AA

Consequences

The genotype detected in the genes studied, considered globally, is associated with a risk corresponding to the majority of the population.

Recommendations

Despite having a similar risk to the majority, bruxism is still very present (50% of the population of Spain); to help reduce it:

• It is important to do **sport on a regular basis** to reduce cortisol levels and reduce stress and anxiety.

• To perform **relaxing activities** such as meditation, yoga or pilates.

• To help **muscle relaxation**, it is recommended to receive **body massages** to relieve general stress.

• The use of **dental relief plates** helps to avoid tooth wear due to bruxism.

Periodontitis
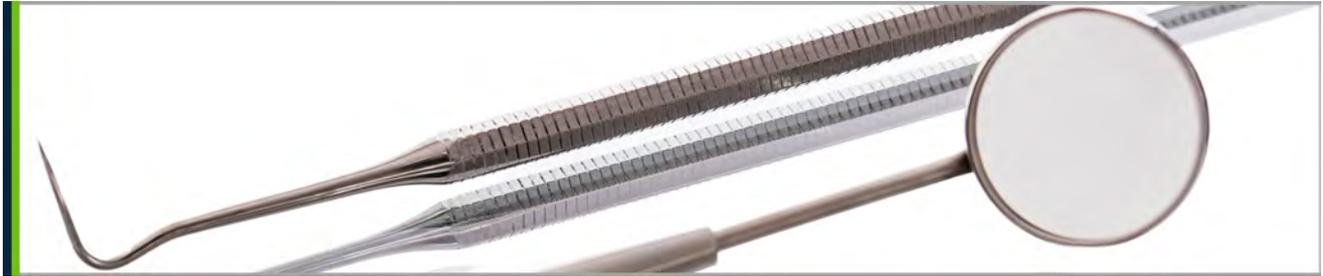
Periodontitis consists of an **inflammatory destruction** of the tissues around the teeth. This destruction promotes **bacterial colonization**, which in turn **increases inflammation**. It is a complex mechanism involving inflammatory factors, immune system proteins and other receptors. This disease results in loss of masticatory function, aesthetic alterations and ultimately, if left untreated, exfoliation of the teeth.

Periodontal disease is **frequent**, it increases with age and, after the age of 50, it affects more than 50% of the population. Therefore, its **prevention is very important** in global health. The basic measures are dental hygiene and people with more **genetic risk** should be recommended **stricter** guidelines.

Cytokines, such as interleukins (IL) or tumor necrosis factor (TNF), are proteins **released by the immune system** that play a fundamental role in the regulation of the inflammatory response. **Polymorphisms** are known that affect their level of expression, thus affecting **genetic susceptibility to inflammatory processes**, such as periodontitis. The most important in this case are: **IL1A**, **IL1B**, **IL18**, **IL6** and **TNF-A** (**proinflammatory**) and **IL10** (**anti-inflammatory**).

Other proteins are also involved in the mechanism of periodontitis. Among them is the **vitamin D receptor** (VDR). This vitamin contributes to the maintenance of good oral health, but depends on its receptor to produce a physiological effect. Some variants of its gene alter its expression and, thus, the protective effect of vitamin D.

Finally, extracellular **matrix metalloproteinases** (MMPs) are proteins that **degrade** extracellular matrix components, such as collagen, during the development of inflammation. MMP-9 is abundantly expressed in gingival tissues and an **imbalance between MMPs** and their inhibitors is responsible for the destruction process of structural proteins and tissues during periodontitis.
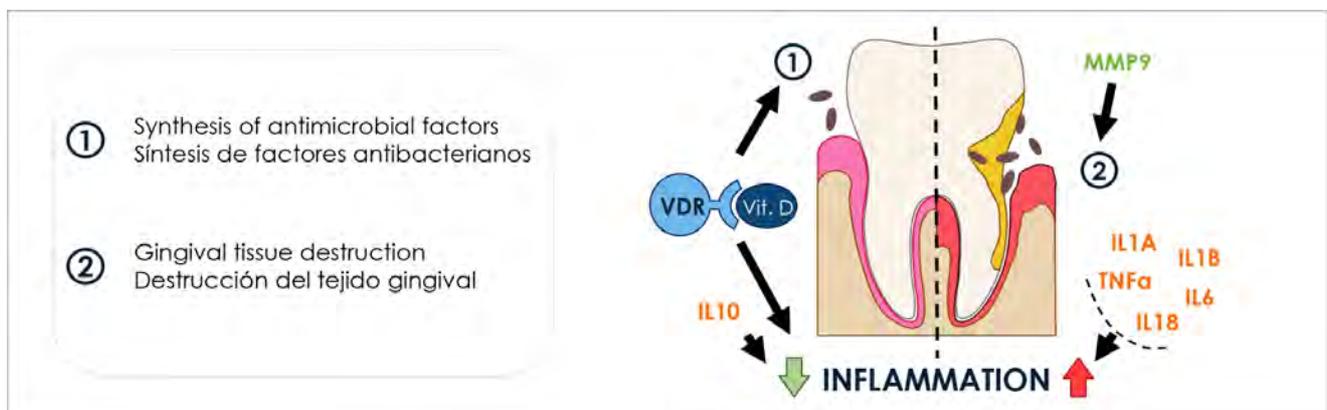
Gene	Rs Number	SNP	Results
IL10	rs1800896	-1082G›A	CT
IL10	rs1800872	-592T›G	TG
IL18	rs187238	-137C›G	CC
IL1A	rs1800587	-889G›A	AG
IL1B	rs1143634	315C›T	GG
IL6	rs1800796	85+369G›C	GC
IL6	rs1800795	-174C›G	CC
MMP9	rs3918242	-1562G›A	GG
TNFa	rs1800629	-308G›A	AG
VDR	rs731236	TaqI	AA

Consequences

The genotypes detected in the studied genes is associated with a global genetic risk that corresponds to the majority of the population.

Recommendations

The genotypes detected are associated with an **average or normal risk** of suffering periodontitis. Despite not having a higher risk, it is recommended to follow a correct oral hygiene and an anti-inflammatory lifestyle.

To maintain proper oral health:
• **Regularly visit the dentist** for detect signs of periodontitis as early as possible.

• **Brush your teeth twice a day** for 2 minutes with a soft toothbrush, **brush your tongue** and **clean interdental spaces** with interdental aids (such as dental floss or interproximal brushes).

• It is essential to **avoid smoking**, as it increases the risk of oral infections.

• It is best to use **fluoride toothpastes**.

To reduce inflammation:
• **Avoid unhealthy weight gain** and obesity.

• **Follow an anti-inflammatory diet** rich in antioxidants present in fruits and vegetables.

• **Increase consumption of omega-3** PUFA and **avoid trans fats and ultra-processed foods**.

• **Perform moderate exercise** on a regular basis, **reduce stress** and try to have a good rest.

• **Avoid excessive alcohol consumption**.

Periodontitis - Risk factors

Genetic polymorphisms are a very important factor in predicting the risk of periodontitis. However, there are also non-genetic factors, which may increase the risk, that can be acted upon to prevent periodontitis. These factors include:

Smoking	Poor oral hygiene	Diabetes	Prolonged stress	Elevated oestrogen levels

Periodontitis - Risk factor for other pathologies

The importance of preventing and treating periodontitis is not only because of the effects of this specific pathology, but also because as an inflammatory pathology that promotes the synthesis of interleukins, it has been associated with an increased risk of cardiovascular pathology and rheumatoid arthritis of inflammatory origin.

CARDIOVASCULAR PATHOLOGY

Cardiovascular diseases are a group of disorders of the heart and blood vessels. They are the leading cause of death in developed countries.

Periodontitis increases the overall infectious and inflammatory burden of our body and may contribute to cardiovascular events and strokes in susceptible individuals.

Many studies support the link between periodontitis and cardiovascular risk. Despite some common causes, such as smoking, which sometimes make statistical interpretation difficult, the *European Workshop Periodontology* insists on the importance of further research.

It is therefore important to prevent the onset of periodontitis in order to avoid its effects on the cardiovascular system.

RHEUMATOID ARTHRITIS

Rheumatoid arthritis is a systemic autoimmune inflammatory disease characterised by persistent inflammation of the joints, preferably the knee, hands and feet, leading to their progressive destruction.

Periodontitis, as an inflammatory process, increases the risk of arthritis by common mechanisms of interleukin and antibody secretion. Therefore, if periodontitis is not treated early, it may contribute to an increased susceptibility to rheumatoid arthritis.

Bibliography selection

To create this report, we have been reviewed contrasted scientific publications , which are available upon request. Below there is a selection of the most relevant ones.

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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.