ID: 00000000000

Genetics for people

Genetic Testing Food Intolerances

My i4

Coeliac disease

Low risk

Lactose

Low risk

Fructose

Low risk

Histamine

Low risk

Coeliac disease

Gluten Intolerance - Coeliac Disease

Low risk 

1- Information about Coeliac Disease

Permanent gluten intolerance is a chronic, autoimmune, inflammatory disorder of the small intestine known as **Celiac Disease (CD)** that occurs in individuals genetically predisposed to the risk haplotypes of the human leukocyte antigen (HLA).

2- Your Result

HLA-DQ2 and HLA-DQ8 haplotypes are the genetic markers that indicate the genetic predisposition that increases the likelihood of CD. The HLA-DQ2 allele is present in 90-95 % of celiac patients, while the remaining 5-10 % have the HLA-DQ8 allele. The risk haplotypes are reflected in the table Risk classification.
The estimated prevalence in people of European origin is 1 %, being more frequent in women with a 2:1 ratio.

Markers	Your haplotype
HLA-DQ2	DQ-/DQ-
HLA-DQ8	

3- Conclusion of your test

You have a **Low Genetic Predisposition** to be celiac. Therefore, although it does not mean that you will suffer from Celiac Disease, there is a possibility, albeit low, that you will develop it.
In **Annex I**, you will find information on the disease's main symptoms and a list of foods that can be harmful. If you recognize some of the symptoms, it may be advisable to see a specialist doctor for more information and other tests to confirm the diagnosis. It should be noted that there are other gastrointestinal diseases related to discomfort caused by gluten, which are not determined by genetic analysis. If you have a positive diagnosis for Celiac Disease, we recommend that you consult a dietician to help you adjust your diet accordingly.

Risk classification:

Haplotype	Risk level
DQ2.5 / DQ2.5 DQ2.2 / DQ2.5 DQ2.2 / DQ7 DQ2.5 / DQ8 DQ2.2 / DQ8	High
DQ8 / DQ8 DQ2.5 / DQ7 DQ2.5 / DQ- DQ8 / DQ7 DQ8 / DQ- DQ2half	Moderate
DQ2.2 / DQ2.2 DQ2.2 / DQ- DQ- / DQ7 DQ7 / DQ7 DQ- / DQ-	Low

Lactose

Primary Lactose Intolerance - Acquired Hypolactasia

Low risk

1- Information on Acquired Hypolactasia

Primary Lactose Intolerance, also known as **Acquired Hypolactasia**, is genetically determined and is a normal and majority metabolic condition in humans (70 % of the world's population). Specifically, 40 % of the population of European origin is lactose intolerant, this value increases to more than 70 % in the case of Asian, Arab, African and African-American populations.
La **LACTASE** is the enzyme responsible for hydrolysing lactose (the milk sugar) and promoting its absorption and digestion. This enzyme naturally loses its activity and becomes non-functional with age. This is why Acquired Hypolactasia, also known as **NON PERSISTENT LACTASE**, is an ancestral condition common in all mammals and is characterised by a **deficit of the intestinal enzyme LACTASE** (hypolactasia).
Despite this, there is a small percentage of the world's population that has a **PERSISTENT LACTASE** or, in other words, **possesses a functional LACTASE enzyme** that allows them to digest lactose normally and benefit from its consumption.

2- Your Result

At the genetic level, 5 single nucleotide polymorphisms (SNPs) associated with the Persistent Lactase phenotype are currently known, two of which are more frequent in populations of Caucasian origin (C/T-13910 and G/A-22018) and the other three in populations of African origin (C/T-14010, T/G-13915 and C/G-13907). All these SNPs are present in the sequence of the *MCM6* gene, a gene that regulates the expression of LACTASE.
The test covers the analysis of the presence or absence of these 5 protective SNPs against lactose intolerance.

Polymorphism	Your genotype
C/T-13910	AA
G/A-22018	TT
G/C-14010	CC
T/G-13915	AA
C/G-13907	GG

3- Conclusion of your test

You have a protective genotype for several polymorphisms of the *MCM6* gene, associated with the **PERSISTENT LACTASE** phenotype, which favor your ability to digest lactose.
This fact means that you have a **Low Risk** of suffering from a reduction in LACTASE levels and developing permanent lactose intolerance throughout your life.
However, you can also suffer from transient lactose intolerance caused by the alteration of the intestinal microbiota. The intestinal microbiota composition can be altered by factors such as diet, chronic inflammatory diseases, stress, diarrhea or constipation, and drug use.
In any case, we recommend you ask for more information from your gastroenterology specialist about the disease if you have any of the symptoms specified in **Annex II** .

Fructose

Hereditary Fructose Intolerance - Fructosemia

Low risk

1- Information on Fructosaemia

Hereditary Fructose Intolerance (HFI), or fructosemia, is an inherited congenital disorder caused by disruption of the aldolase B (*ALDOB*) gene, which results in the inability to metabolise foods containing fructose, sucrose and/or sorbitol.
As it is a genetic disease, even if you do not have the disease, you may be a carrier of the genetic risk variants and these may be expressed in your offspring.
IHF is not due to fructose malabsorption in the small intestine, but is due to a metabolic malfunction which, if undiagnosed, can have serious consequences.

2- Your Result

The *ALDOB* gene can have different mutations responsible for the disease, but seven of them are responsible for more than 90 % of IHF cases. The test covers the analysis of these mutations. For an individual to have the disease, he or she needs to carry two copies of the same mutation, i.e. homozygous, or one copy of at least two mutations, i.e. heterozygous.

Mutations	Your genotype
R60X	GG
D4E4	II
A150P	CC
A175D	GG
Y204	AA
N334K	GG
W148R	AA

3- Conclusion of your test

You do not have the risk genotype in any of the seven main mutations of the ALDOB gene. Since you must be homozygous (2 copies) for one mutation or heterozygous (1 copy) of at least two mutations, it is very unlikely that you have Hereditary Fructose Intolerance (HFI). However, although the frequency of other mutations is very low compared to the seven main mutations, the possibility that you have a minor mutation cannot be totally ruled out. Therefore, your genetic predisposition is classified as **Low Risk**.

Histamine

Histamine Intolerance - Food Histaminosis

Low risk

1- Information about Histamine Intolerance

Histamine intolerance is a disorder caused by the body's inability to break down histamine in the gut. This leads to its accumulation in plasma and binding to histamine receptors throughout the body, causing a wide range of symptoms.

2- Your Result

Histamine degradation is mainly carried out by the enzyme diamine oxidase, or **DAO**, present in the gut and encoded by the gene *AOC1*. There is a complementary pathway in which the enzyme N-methyltransferase or **HNMT** is responsible for its degradation. Polymorphisms in the genes coding for these enzymes affect their activity, **reducing their ability to degrade histamine**.

Gene	Polymorphism	Your genotype
AOC1	rs10156191	CT
	rs1049742	CT
	rs2268999	AT
	rs1049793	CG
	rs2052129	GT
HNMT	rs1050891	AA
	rs11558538	CC

3- Conclusion of your test

You do not present **any significant alteration** in the activity of DAO or HNMT. Therefore, you present a **low genetic predisposition** to suffer adverse effects as a consequence of histamine.
In the **annex IV** you will find information about the main symptoms of the disease and a list of foods that can be harmful, as well as the drugs that can affect histamine metabolism. If you recognise some of the symptoms, it may be advisable to see a specialist doctor for further information and tests to confirm the diagnosis. If you have a positive diagnosis of histamine intolerance, we recommend that you consult a dietician to help you adjust your diet accordingly.

Enzyme	Activity
DAO	Normal
HNMT	Normal

ANNEX I: Coeliac disease

1- Síntomas frecuentes

The symptoms are very diverse, yet most are related to the digestive system. Some people are asymptomatic and may not feel any discomfort.

 BABIES	 CHILDREN	 TEENAGERS	 ADULTS
Vomiting Chronic Weight loss Irritability	Bloating and/or pain abdominal diarrhoea Fatigue Apathy Stunted growth	Digestive problems Loss of appetite Menstrual irregularities Failure to thrive	Infertility Repeated miscarriages Anaemia Osteoporosis Depression Dermatitis herpetiformis Mouth sores

2- Classification of gluten-containing foods

FOODS CONTAINING GLUTEN	FOODS THAT MAY CONTAIN GLUTEN	GLUTEN-FREE FOODS*
· Bread, cereals and flour made from wheat, barley, rye, triticale and kamut® · Manufactured products containing any of the above-mentioned flours in any form (starches, meal, semolina, proteins, etc.) · Uncertified and/or unsafe oats · Pasta food: noodles, macaroni, tagliatelle, etc · Distilled or fermented beverages made from cereals: beer, barley water, etc · Buns, cakes and pies · Buns, cakes and pies · Communion wafers	· Dried figs · Nuts, roasted or fried with flour and salt - Canned fish in sauce, with fried tomato - Canned meat, meatballs, hamburgers - Sausages: chopped sausage, mortadella, chorizo, black pudding, sausages, etc. - Melted cheeses, spreads and special cheeses for pizzas - Pâtés - Sauces, condiments and food colourings - Ground spices - Coffee, chocolate and cocoa substitutes and other machine-made beverages - Certain types of ice cream - Candies and sweets	· Fruits - Vegetables and tubers - Rice, maize, tapioca and their derivatives - Pulses and legumes - Natural dried fruit and nuts - Fish and shellfish, fresh, frozen, uncoated, canned, uncoated or in oil - Eggs - All types of fresh, frozen and canned meat and offal - Sausages: cecina, serrano ham and cooked ham of extra quality - Milk and dairy products - Salt, wine vinegar, spices in branches, grains and all natural spices - Oils and butter - Coffee beans or ground coffee, herbal teas and orange, lemon and cola soft drinks - Wines and sparkling beverages - Sugar and honey

* International symbol indicating **gluten-free food**, currently regulated by the European Coeliac Society (AOECS).

Certain medicines may contain gluten as an excipient. In these cases, the pharmaceutical company is obliged to state this in the package leaflet.

ANNEX II: Acquired hypolactasia

1- Frequent symptoms

GASTROINTESTINAL SYMPTOMS	EXTRAINTESTINAL SYMPTOMS
Abdominal pain (~100 %)	Headache (86 %)
Abdominal distention (~100 %)	Lack of concentration(82 %)
Dizziness (~100 %)	Muscle pain (71 %)
flatulence (~100 %)	oint pain/stiffness (71 %)
Vomiting (78 %)	Asthenia (63 %)
nausea (78 %)	mouth ulcers (30 %)
Diarrhoea (70 %)	Increased frequency of urination (<20 %)
Constipation (30 %)	

2- Classification of lactose-containing foods

LACTOSE-CONTAINING FOODS*	FOODS THAT MAY CONTAIN LACTOSE	ALIMENTOS SIN LACTOSA
Milk of animal origin (including breast milk), milk powder, evaporated milk, condensed milk, milk shakes, butter, cream, yoghurt, fresh cheese, fermented or cured cheese, cream, curd, dairy desserts, puddings, custards, rice pudding, mousse, ice cream, béchamel sauce, milk chocolate **Ingredients:** Lactose, lactose monohydrate, milk sugar, milk solids, whey, buttermilk or whey, milk fats **Aditives:** E966 Lactitol	Creams, soups, breads, cakes and pies, cold cuts, sausages, fried meats, purees (potato, vegetable, etc.), pastries (doughnuts, muffins, buns, etc.), biscuits, pancakes, toast, ready meals, enriched cereals, salad dressings, mayonnaise, ice cream sorbets, milkshakes, batter, chocolate substitutes, instant soups, fermented or distilled alcoholic beverages, margarine **Products:** Excipients in medicines, vitamin complexes, toothpastes, etc **Ingredients:** Rennet	Natural fruit, nuts, fish, seafood, cereals, eggs, honey, jam, potatoes, rice, pasta, vegetables, pulses, white and red meat, vegetable drinks (soya, coconut, oats, rice, etc), vegetable milk. **Ingredients of dairy origin:** Milk protein, casein, caseinate, calcium caseinate (formerly additive H/E4511), sodium caseinate (formerly additive H/E4512), potassium caseinate (formerly additive H/E 4513), magnesium caseinate, protein hydrolysate, lactalbumin, lactalbumin, lactoglobulin **Aditives:** E101 Riboflavin or Lactoflavin, E101A Riboflavin or Lactoflavin phosphate, E106 Lactoflavin phosphate, E270 Lactic acid, E325 Sodium lactate, E326 Potassium lactate, E327 Calcium lactate, E328 Ammonium lactate, E329 Magnesium lactate, E585 Ferrous lactate, E415 Xanthan Gum, E418 Gellan Gum, E472b Lactic acid mono and diglyceride fatty acid esters, E575 Glucono Delta Lactone, E480 Sodium Dioctyl Sulfosuccinate, E481 Sodium Stearoyl 2-Lactylate, E482 Calcium Stearoyl 2-Lactylate, E963 Tagatose

* All products containing lactose must be clearly labelled as such.

ANNEX III: Fructosaemia

1- Frequent symptoms

SYMPTOMATOLOGY			
Nausea	Convulsions	Drowsiness	Shakiness
Vomiting	Growth retardation	Abdominal pain	Hypoglycae-mia

2- Classification of foods containing fructose, sucrose and/or sorbitol

FOOD	NOT RECOMMENDED	LIMITED FOOD 2-3 veces/semana	PERMITTED FOODS
Dairy and dairy products	Dairy products with added sugars (milk shakes, ice cream, fruit, vanilla and flavoured yoghurts), infant formulas with sucrose, fructose or honey, cheese spreads (with herbs, garlic, nuts, mushroom and/or fruit)	Unsweetened Greek yoghurt, unsweetened soya drink	Breast milk, cow's milk, unsweetened evaporated milk, powdered milk, fermented milks without added sugar, butter, margarine, natural yoghurt, cheese, cottage cheese
Meat, fish and eggs	Processed meats, raw sausages, cured sausages (salami, black pudding), foie gras, cooked ham, fish surimi and any other meat where sugar is used in its production		Beef, chicken, lamb, pork, rabbit, turkey, horse, offal, fish and seafood, cured ham, bacon, bacon, bacon, egg
Fruits	Other fruit	Prickly pear, lime, lemon	Avocado, papaya, black olives
Vegetables and legumes	Carrots, pumpkin, sweet potato, onion, turnip, corn kernel, beetroot, parsnip, peas, sweet corn, soybean, white bean, chickpea, sweet potato	**From 2 to 6 years old:** 1 portion of 50g. **From 6 to 10 years old:** 100g serving of new potato, radish, cucumber, courgette, aubergine, asparagus, artichoke, kale, brussels sprouts, tomato, red cabbage, green beans, cauliflower, parsley, chives, green pepper, leek, lentils	**Up to 2 years:** 50-100g/day ration of old potato, tapioca, spinach, mushrooms, bamboo shoots, cabbage, lettuce, celery, endive, chard, broccoli, endive, tofu
Cereals and derivatives	Bran, wheat germ, all breads, cereals and biscuits with wheat germ or bran sugar (wholemeal varieties), biscuits, desserts, pastries, buns, soy flour		Rice, wheat, rye, oats, semolina (not wholemeal), maize flour, wheat, rice, pasta, unsweetened white bread, fructo-oligosaccharide-free and wholemeal infant cereal porridge.
Fats and oils	Mayonnaises, mustards and any commercial sauces produced with sugar		Vegetable oils, butter, margarine, mayonnaise and mustard prepared without added sugars
Beverages	Instant teas, drinking chocolate, malted milk drinks, fruit and/or vegetable juices, soft drinks, diabetic beverages with sorbitol or fructose, tonic		Tea, coffee, cocoa, herbal teas, mineral water, soft drinks sweetened with saccharin or aspartame (without sugar or fruit flavourings)
Desserts and sweeteners	Honey, white and brown sugar, jams, marmalades, chocolates, jams, quince jelly, candies, syrup, dietary products containing glucose, dextrose, dextrin, maltose and zero-calorie products.		Chocolate with no added sugars with permitted sweeteners, sugar-free chewing gum and candies with permitted sweeteners)
Nuts	Nuts		Sesame seeds, pumpkin seeds and sunflower seeds (max. 10g/day)
Other	Ice cream, Modena vinegar, ketchup, vanilla flavoring		Yeast, spices and aromatic herbs, white vinegar, salt, pepper

It should be noted that, in addition to fructose, sucrose and sorbitol, other ingredients or excipients of medicinal products may give rise to fructose or sorbitol.

ANNEX IV: Histamine Intolerance

1- Frequent symptoms

GASTROINTESTINAL SYMPTOMS	EXTRAINTESTINAL SYMPTOMS	
Abdominal Distension	Headache and Migraine	Hypotension
abdominal pain	dizziness	hypotonia
Bloating	Menstrual cramps	Fainting spells
Flatulence	Pruritus	Nasal Congestion
Diarrhea	Dermatitis	Sneezing
Constipation	Hives	Runny nose
Nausea	Facial Erythema	Rhinitis
Vomiting	Tachycardia	Dyspnoea

2- Classification of histamine-containing foods

FOODS WITH HIGH HISTAMINE CONTENT	MEDIUM-HIGH HISTAMINE FOODS	FOOD CONSIDERED SAFE
Canned or fermented fish, cured and semi-cured cheeses, grated cheese, fatty fish, alcoholic and fermented beverages, citrus fruits, dry fermented meat products, spinach, tomatoes, sauerkraut, strawberries.	Seafood, eggs, fermented soya derivatives, aubergine, avocado, banana, kiwi, chocolate, nuts, milk, lentils, mushrooms, chickpeas, soya.	Water, coffee, bread, pastries, potatoes, rice, pasta, cereals, millet, buckwheat, corn, lettuce, chicory, carrots, garlic, onion, cucumber, pumpkin, courgette, pepper, radish, artichoke, rhubarb, asparagus, chicory, apple, pear, cherries, peach, apricot, watermelon, blueberries, spices and herbs, vegetable oil, vinegar, fresh or immediately frozen meat and fish, boiled eggs, fresh boiled ham, marmalade and juices of permitted fruits and vegetables, honey, butter, margarine.

3- Drugs involved in histamine metabolism

FÁRMACOS					
Acetylcysteine	Amiloride	Chloroquine	Doxycycline	Marcaine	Promethazine
Acetylsalicylic Acid	Aminophylline	Codeine	Fetidine	Metamizole	Propafenone
Ascorbic Acid	Amitriptyline	Cholisti-methate	Furosemide	Metoclopramide	Quinidine
Clavulanic acid	Barbiturates	Cycloserine	Haloperidol	Morphine	Suxametho-nium
Acriflavin	Cefotiam	Tubocurarine	Hydralazine	Neomycin B	Theophylline
Alcuronium	Cefuroxime	Diazepam	Ibuprofen	Pancuronium	Thiamine
Radiocontrast agents	Cyclophospha-mide	Diclofenac	Monoamine oxidase-1 inhibitors	Pentamidine	Thiopental
Alprenolol	Cimetidine	Dobutamine	Isoniazid	Prilocaine	Verapamil
Ambroxol	Clonidine	Dopamine	Lidocaine	Procaine	

ANNEX V: Links of interest

1- Coeliac Disease

For more information about **Coeliac Disease** you can access any of the following links:

- Federation of Coeliac Associations of Spain (FACE): celiacos.org
- 'Early Diagnosis of Coeliac Disease' of the Spanish Ministry of Health, Social Services and Equality: mscbs.gob.es
- Study on the situation of people with coeliac disease in Spain: defensordelpueblo.es

2- Primary Lactose Intolerance

For more information about **Primary Lactose Intolerance** you can access any of the following links:

- Association of lactose intolerant people Spain (ADILAC): lactosa.org
- "Update on Lactose Intolerance" by the Spanish Digestive System Foundation. (FEAD): Lactose Intolerance Update
- Sociedad Española de Gastroenterología, Hepatología y Nutrición Pediátrica (SEGHNP): seghnp.org

3- Fructosemia

For more information about **fructosaemia** you can access any of the following links:

- Association of People Affected by Hereditary Fructose Intolerance (AAIHF): aaihf.com
- "Manual for the feeding of patients with inborn errors of metabolism" of the Spanish Society of Paediatric Gastroenterology, Hepatology and Nutrition. (SEGHNP): Manual for the feeding of patients with inborn errors of metabolism
- Sección de Gastroenterología, Hepatología y Nutrición infantil. Hospital Sant Joan de Déu: metabolicas.sjdhospitalbarcelona.org

4- Histamine Intolerance

For more information about **Histamine intolerance** you can access any of the following links:

- Histamine Intolerance Awareness: histamineintolerance.org.uk
- Sociedad Internacional del Déficit de DAO: deficitdao.org

5- Other

Other links of interest:

- Agencia Española de Seguridad Alimentaria y Nutrición (AESAN): aecosan.msssi.gob.es

TECHNOLOGY

DNA Microarray technology consists of a solid surface with microscopic reactions (micro-reactions) or DNA chips on which molecular probes are attached to detect the presence of target DNA molecules. Probe-target hybridisation is usually detected and quantified by measuring the intensity of a specific fluorescence provided by the molecular probe in the samples. This type of technology allows the detection of thousands of specific DNA fragments present in a DNA sample. On the other hand, the specificity in terms of DNA sequence recognition is very high, as single nucleotide exchange (single base resolution) can be detected using short oligonucleotide probes (20-25 nucleotides). As a consequence, DNA Microarray technology has also evolved to be applied as a DNA sequencing technique to genotype several hundred thousand single nucleotide variants (SNVs) in target genes located throughout the genome (hole genome DNA Microarray).

Bead Chip Infinium Global Screening Array Orion (GSA Orion) is a line of DNA chips developed by Illumina for its iScan DNA Microarray platform, widely used in population genetic studies and precision medicine, providing optimised content with high quality, 100 percent reliable and reproducible genotyping results. The construction of the GSA Chip was carried out in collaboration with a consortium of experts and the selection of SNVs, using information from renowned scientific databases such as gnomAD, NHGRI-EBI-GWAS Catalog, ClinVar, MHC-HLA-KIR and PharmGKB. GSA allows the analysis of approximately 700,000 SNVs covering variants of interest (hot spots) across the entire genome, with impact on a wide range of genetic traits with physiological and pathophysiological implications. In addition, it allows customisation by users to incorporate 50,000-100,000 variants of interest.

RISKS AND LIMITATIONS

The results presented in this report are limited to the scientific knowledge existing at the date of preparation of this test. Overgenes guarantees the accuracy of the scientific knowledge, the highest association with the tested intolerances is presented in the report. The test only detects the specified genetic variants. In the case of primary lactose intolerance, the A-22018 polymorphism has been described as protective in the European population when associated with the T-13910/A-22018 haplotype, however, it has been described as protective independently of T-13910 in other populations. The A-22018 polymorphism has scientific evidence but not as extensive as the other polymorphisms in the analysis. The test does not perform the study of congenital lactasia or secondary or transient hypolactasia.
In the case of IHF, the test screens for the mutations most frequently described as causing IHF (90 %). As it is a screening test, the presence of other rare mutations in the *ALDOB* gene cannot be ruled out, so if clinical suspicion of IHF persists, it is recommended to perform an extended analysis of the gene. If two mutations are detected in the *ALDOB* gene, the test cannot differentiate between cis and trans configuration, i.e. it does not differentiate whether both mutations are located in the same copy of the gene or whether each mutation is located in one of the copies. In order to perform this discrimination, it is necessary to analyse a sample of the parents.
. In the case of histamine intolerance, the test analyses genetic variants of the enzymes responsible for its degradation. There are other causes that can affect the activity of these enzymes or that can trigger histamine reactions, so if there is a suspicion of this intolerance, it is recommended that a specialist be consulted.

GLOSSARY

- **Allele:** both copies of a gene, which may differ in sequence.
- **Phenotype:** a set of observable characteristics of an organism.
- **Genotype:** a combination of the variants of a gene in an individual.
- **Haplotype:** a set of DNA variations, or polymorphisms, that tend to be inherited together.
- **Heterozygous:** when the two alleles of the same gene are different.
- **Homozygous:** when the two alleles of the same gene are the same.
- **Mutation:** variation in the nucleotide sequence of genes affecting 1% of the population.
- **Polymorphism:** nucleotide sequence variation in the genes affecting the population.
- **SNP:** single nucleotide genetic polymorphism.

Genetics for people

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