Codigo Prevention

Hello, User!

Welcome to your genetic code!

YOUR DNA PROFILING FOR PREVENTION OF DISEASES

We present to you the results of your DNA profiling for disease prevention according to the genotyping test. The following report contains information about the genetic variants that we found in your genome and have been associated, according to medical and scientific studies, with a potential increased risk of an individual to develop specific diseases throughout his/her life.

In this report we have calculated a parameter for your predisposition or risk to develop some diseases according to your genotype. Our quantitative analysis includes markers for Alzheimer's disease, Parkinson's disease, diabetes, breast cancer, ovarian cancer, prostate cancer, some common metabolic diseases such as: congenital hypothyroidism, cystic fibrosis, tyrosinemia, etc.

You must take into account that the results of this genetic analysis do not contain information for all the genetic variants known in the human genome. This is due to the ongoing discovery of new variants associated with specific diseases in research studies under development.

In this study we analyzed about 600,000 genetic variants distributed among your 23 pairs of chromosomes. Our genetic test mainly analyzes single nucleotide variants (SNVs) and some small deletions and insertions (INDELs) in your genomic DNA. Due to the number and the genomic distribution of the variants analyzed by Código 46, this study is useful to know, in general terms, a large number of diseases associated with these markers. This report includes information of variants classified as pathogenic or high risk in the database of clinical variants (ClinVar) of the National Center for Biotechnology (NCBI) of the United States of America.

It is our responsibility to inform you that even when you have a predisposition or risk to certain diseases associated with some genetic markers, it does not mean that you are going to develop a disease. There are other non-genetic factors such as: nutrition, lifestyle, environment or stress, etc., which may be related to the development of the described health conditions.

Below you will find a section entitled How to read your report. This section will serve you as a guide to read the sections of the document and the information that each one contains. At the end of this report you will find two other sections; the first one specifies the limitations of the test and the second one contains a glossary that you or your doctor can use as a complement to read the information contained in the test.

HOW TO READ YOUR PREVENTION REPORT

The disease prevention report contains several sections, each corresponding to different health conditions for which associations were found with the variants studied in your genome. In turn, each of the sections is divided into additional parts.

There is a brief description of the disease studied at the beginning of each section for each disease. After this brief description, a summary table appears with data associated with your genotype and the general characteristics of the variants detected in your genome; the affected gene, the identifier of the variant (dbSNP), your personal genotype for the variant in the two chromosomes, the number of the chromosome in which the variant is located, the position of the variant within the chromosome and the state of the variant analyzed in your two chromosomes. If they are in a homozygous or heterozygous state.

With the information from you allelic variants, we can approximate the risk grade you have to develop the reported diseases, with two distincts parameters. The first, of these parameters, is known as Lifetime Risk or LTR, while the second is known as Disease Risk Score or DRS.

LTR parameter is based on statistic data at population level and include the multiple factors from the disease can occur. Within these factors, your LTR score indicates the incidence you have, throughout your lifetime, within the number of inhabitants with a risk profile similar to yours.

DRS parameter is based on comprehensive studies that associate the effect level of an observed allelic variant in a particular trait. Some genetic variants would have either a major or minor effect in comparison. With such studies, it is possible to approximate an overall genetic score regarding all the variants found in your genotype. Therefore, your DRS indicates the odd risk because of the overall quantitative effect of all the variants found in your genotype.

To ease the interpretation of these parameters, we have harmonized the parameter units to help you understand the values of risk in your genetic context (DRS) and in the epidemiological context (LTR) respect to the overall population .

LTR interpretation scale is expressed in terms of a given population segmentation. If your LTR score is, for example, 1 out of 15 for a given disease, it means that the risk of developing a disease is observed in 1 person from a subset of 15, with a similar population profile. The smaller the LTR is, the greater the risk of incise in the trait of the profile.

DRS score scale is expressed in terms of a base-2 exponential function. So, whether your risk score is, for example, 1.0 for a given trait, it means that your genetic risk is 2 times more likely to suffer such disease. When your risk score is negative, it implies that your genetic risk score is lesser, in terms of the same value (If it is -1.0, you have 2 times lesser risk). When your risk score si zero, it means that your genetic risk does not increase nor decrease the risk of suffer the given disease. In order to understand this risk score, we help you to visualize it graphically

After the summary table, a qualitative description of the pathogenic variants that we detect in your genotype appears. We consider it important to give you more details about these variants because for these a direct association with the development of the disease has been found and reported. After part, it is displayed a section that contains a list of the molecular and physiological functions of the proteins encoded by the genes affected by your genetic variants. If your genetic test reveals the existence of more than one disease variant associated with the same gene or multiple genes, these will be listed as well in a list. There are times when a particular variant can cause more than one disease. If this is the case, the additional health conditions associated with the variant will be described in the form of a list in a dedicated section. After the sections that describe the variants, genes and other diseases associated with the variants, another section appears with additional details of the risk parameters you have for the disease. That is, you will find a broader description of the LTR for people of your age in the population and the DRS that we calculated given your genetic variants analyzed.

We recommend that you go with a medical professional if you have any risk for any condition reported here, if any member of your family has any of the diseases analyzed or if you have any questions about the results of your genetic test. It is important that you be more careful with your health if any of the risk variants analyzed were detected in your genotype. Keep in mind that not having any of the risk variants analyzed does not mean that the disease under study will not be developed. There are other genetic risk markers that are not included in this analysis and continue in research. Take into account that other non-genetic factors can also affect your risk of developing a disease.

This genetic analysis can not determine with total certainty if you are going to present a health condition in the future. This study offers you a probabilistic estimate of presenting a disease given the population risk of the disease and a set of variants that we analyze in your genotype. This study offers you an overview of your health given certain genetic variants of risk; however, it should not be used to make decisions without medical consultation.

DISEASE PREVENTION REPORT

Diabetes

Diabetes mellitus (DM) is a group of metabolic disorders, whose main characteristic is the presence of high concentrations of glucose in the blood persistently or chronically, due to either a defect in the production of insulin, a resistance to the action of it to use glucose, an increase in the production of glucose or a combination of these causes. It is also accompanied by abnormalities in the metabolism of lipids, proteins, mineral salts and electrolytes.

Código 46 looks for pathogenic variants in your genome, these variants are directly related to the development of such disease. When the number of pathogenic variants detected is 0, it means that you do not have mutations that have already been clinically reported in patients who develop that disease. On the other hand, for some diseases, DRS is also calculated, which serves to compare a profile of variants with respect to populations, whether healthy or sick. Therefore, the number of pathogenic variants and the DRS are independent measurements.

Abstract Pathogenic variants Tested 20 Detected 4

Risk parameters LTR 1/2 DRS 3.028

Gene	Variant	Genotype	Chromosome	Position	Condition
GCK	rs193922338	A/T	7	44186137	Heterozygous
GCK	rs193922335	T/A	7	44186210	Heterozygous
ZFP57	rs77625743	C/T	6	29641145	Heterozygous
HNF1B	rs121918673	G/C	17	36061127	Heterozygous

Characteristics of the genetic variants detected

rs193922338

The variant rs193922338 was detected in a heterozygous state (genotype A/T) in your genome. This variant is located in the position 44186137 of chromosome 7 in an exonic region of the GCK gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 315 the protein, causing a change from leucine to histidine (L315H).

rs193922335

The variant rs193922335 was detected in a heterozygous state (genotype T/A) in your genome. This variant is located in the position 44186210 of chromosome 7 in an exonic region of the GCK gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 291 the protein, causing a change from lysine to termination codon (K291*).

rs77625743

The variant rs77625743 was detected in a heterozygous state (genotype C/T) in your genome. This variant is located in the position 29641145 of chromosome 6 in an exonic region of the ZFP57 gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 248 the protein, causing a change from arginine to histidine (R248H).

rs121918673

The variant rs121918673 was detected in a heterozygous state (genotype G/C) in your genome. This variant is located in the position 36061127 of chromosome 17 in an exonic region of the HNF1B gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 465 the protein, causing a change from serine to arginine (S465R).

Characteristics and functions of the affected genes

GCK

Glucokinase

The GCK gene is located on chromosome 7. The protein encoded by this gene is found exclusively in the liver and pancreas. Participates in the modulation of insulin secretion. In the presence of glucose, the enzyme uses the molecule as a substrate and transforms it into glucose-6-phosphate for the synthesis of glycogen. The low glucose and high fructose-6-phosphate triggers the association with the inhibitor GKRP preventing the function of the enzyme. Mutations and deficiencies in this protein can cause diseases such as: juvenile early-onset diabetes 2 (MODY2), familial hyperinsulinemic hypoglycemia 3 (HHF3), non-insulin-dependent diabetes mellitus (NIDDM), and perioperative neonatal diabetes mellitus (PNMD).

ZFP57

Zinc finger protein 57 homolog

transient neonatal diabetes mellitus 1

HNF1B

Hepatocyte nuclear factor 1-beta

diabetes mellitus type 2

Other pathologies related to the variants found

Scientific reports have shown that the variant rs193922338 is associated with the occurrence of maturity-onset diabetes of the young, type 2. This disease is characterized by having autosomal dominant inheritance pattern.

Scientific reports have shown that the variant rs193922335 is associated with the occurrence of null. This disease is characterized by having autosomal dominant inheritance pattern.

Scientific reports have shown that the variant rs77625743 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs121918673 is associated with the occurrence of null. This disease is characterized by having autosomal dominant inheritance pattern.

Your Diabetes predisposition

Because of set of variants that we detect in your genotype, your risk of having Diabetes is higher than a person randomly chosen from open population.

The lifetime risk (LTR) that a common person has of developing Diabetes is 1/2.

Parkinson's disease

Parkinson's disease (PD), also called Parkinson's disease, idiopathic parkinsonism, agitation paralysis or simply Parkinson's disease, is a chronic neurodegenerative disease characterized by slow movement, stiffness, increased muscle tone and tremor. cognitive function, depression, pain and alterations in the function of the autonomic nervous

system. Parkinson's disease increases its severity over time, as a consequence of the progressive destruction, due to unknown causes, of the pigmented neurons of the substantia nigra.

Código 46 looks for pathogenic variants in your genome, these variants are directly related to the development of such disease. When the number of pathogenic variants detected is 0, it means that you do not have mutations that have already been clinically reported in patients who develop that disease. On the other hand, for some diseases, DRS is also calculated, which serves to compare a profile of variants with respect to populations, whether healthy or sick. Therefore, the number of pathogenic variants and the DRS are independent measurements.

Abstract Pathogenic variants Tested 8 Detected 2

Risk parameters LTR 1/51 DRS -2.0754

Gene	Variant	Genotype	Chromosome	Position	Condition
FBXO7	rs71799110	C/G	22	32889256	Heterozygous
PRKN	rs137853060	T/A	6	162394435	Heterozygous

Characteristics of the genetic variants detected

rs71799110

The variant rs71799110 was detected in a heterozygous state (genotype C/G) in your genome. This variant is located in the position 32889256 of chromosome 22 in an exonic region of the FBXO7 gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 378 the protein, causing a change from arginine to glycine (R378G).

rs137853060

The variant rs137853060 was detected in a heterozygous state (genotype T/A) in your genome. This variant is located in the position 162394435 of chromosome 6 in an exonic region of the PRKN gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 211 the protein, causing a change from lysine to asparagine (K211N).

Characteristics and functions of the affected genes

FBXO7

F-box protein 7

The FBXO7 gene is located in chromosome 22. This gene encodes a member of the F-box protein family which is characterized by an approximately 40 amino acid motif, the F-box. The F-box proteins constitute one of the four subunits of the ubiquitin protein ligase complex called SCFs (SKP1-cullin-F-box), which function in phosphorylation-dependent ubiquitination. Ubiquitin is a small regulatory protein found in most tissues of eukaryotic organisms i.e. it occurs ubiquitously. The addition of ubiquitin to a substrate protein is called ubiquitination. This process affects proteins in many ways: it can mark them for degradation via the proteasome, alter their cellular location, affect their activity, and promote or prevent protein interactions. Mutations and deficiencies on this gene may induce Parkinson disease type 15 (PARK15).

PRKN

E3 ubiquitin-protein ligase parkin

parkinson disease 2

Other pathologies related to the variants found

Scientific reports have shown that the variant rs71799110 is associated with the occurrence of parkinson disease 15. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs137853060 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Your Parkinson's disease predisposition

Because of set of variants that we detect in your genotype, your risk of having Parkinson's disease is lower than a person randomly chosen from open population.

The lifetime risk (LTR) that a common person has of developing Parkinson's disease is 1/51.

Alzheimer's disease

Alzheimer's disease, also called senile dementia of Alzheimer's type, is a neurodegenerative disease that manifests as cognitive impairment and behavioral

disorders. It is characterized in its typical form by a loss of immediate memory and other mental abilities such as higher cognitive abilities. As nerve cells die, different areas of the brain atrophy.

Código 46 looks for pathogenic variants in your genome, these variants are directly related to the development of such disease. When the number of pathogenic variants detected is 0, it means that you do not have mutations that have already been clinically reported in patients who develop that disease. On the other hand, for some diseases, DRS is also calculated, which serves to compare a profile of variants with respect to populations, whether healthy or sick. Therefore, the number of pathogenic variants and the DRS are independent measurements.

Abstract **Pathogenic variants** Tested 2 Detected 2

Gene	Variant	Genotype	Chromosome	Position	Condition
PSEN1	rs63750082	G/C	14	73659420	Heterozygous
PSEN1	rs63750687	C/G	14	73683845	Heterozygous

Characteristics of the genetic variants detected

rs63750082

The variant rs63750082 was detected in a heterozygous state (genotype G/C) in your genome. This variant is located in the position 73659420 of chromosome 14 in an exonic region of the PSEN1 gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 206 the protein, causing a change from glycine to alanine (G206A).

rs63750687

The variant rs63750687 was detected in a heterozygous state (genotype C/G) in your genome. This variant is located in the position 73683845 of chromosome 14 in an exonic region of the PSEN1 gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 381 the protein, causing a change from leucine to valine (L381V).

Characteristics and functions of the affected genes

PSEN1

Presenilin 1

The PSEN1 gene is located on chromosome 14. It is a catalytic subunit of the gamma-secretase complex, an endoprotease complex that catalyzes the intramembrane cleavage of integral membrane proteins, such as Notch receptors and APP (beta amyloid precursor protein). Stimulates cell-cell adhesion via its interaction with other proteins. This protein is required for normal embryionic brain and skeleton development and angiogenesis. Mutations on this gene cause Alzheimer's Disease type 3. Alzheimer's disease is a neurodegenerative disorder characterized by progressive dementia, loss of cognitive abilities and deposition of fibrillar amyloid proteins such as intraneuronal neurofibrillary tangles, extracellular amyloid plaques and vascular amyloid deposits.

Other pathologies related to the variants found

Scientific reports have shown that the variant rs63750082 is associated with the occurrence of alzheimer disease, type 3. This disease is characterized by having autosomal dominant inheritance pattern.

Scientific reports have shown that the variant rs63750687 is associated with the occurrence of null. This disease is characterized by having autosomal dominant inheritance pattern.

Cystic fibrosis

Cystic Fibrosis is an autosomal recessive disorder that affects many different areas of the body including the lungs, digestive system, and reproductive system Signs and symptoms of Cystic Fibrosis start in early childhood and include delayed growth caused by problems in digestion and repeated lung infections that lead to permanent lung damage. Children and adults with Cystic Fibrosis usually have frequent hospitalizations because of lung infections. Over time, complications of Cystic Fibrosis can lead to lung transplants and early death. There are treatments for Cystic Fibrosis that can lessen the severity of the symptoms; however, there is currently no cure.

Código 46 looks for pathogenic variants in your genome, these variants are directly related to the development of such disease. When the number of pathogenic variants detected is 0, it means that you do not have mutations that have already been clinically reported in patients who develop that disease. On the other hand, for some diseases, DRS is also calculated, which serves to compare a profile of variants with respect to populations, whether healthy or sick. Therefore, the number of pathogenic variants and the DRS are independent measurements.

Gene	Variant	Genotype	Chromosome	Position	Condition
CFTR	rs151048781	G/C	7	117243784	Heterozygous
CFTR	rs121908748	G/A	7	117230494	Heterozygous
CFTR	rs79660178	T/A	7	117171045	Heterozygous
CFTR	rs75115087	A/T	7	117232349	Heterozygous
CFTR	rs397508536	A/T	7	117251799	Heterozygous
CFTR	rs77902683	G/C	7	117282622	Heterozygous
CFTR	rs80055610	G/C	7	117227887	Heterozygous
CFTR	rs397508453	G/C	7	117243836	Heterozygous
CFTR	rs121909015	G/C	7	117282647	Heterozygous
CFTR	rs121908748	G/C	7	117230494	Heterozygous
CFTR	rs397508263	G/C	7	117227888	Heterozygous
CFTR	rs121908763	C/G	7	117267694	Heterozygous
CFTR	rs80034486	C/G	7	117292931	Heterozygous
CFTR	rs755416052	A/T	7	117254665	Heterozygous
CFTR	rs149790377	T/A	7	117243667	Heterozygous

Characteristics of the genetic variants detected

rs151048781

The variant rs151048781 was detected in a heterozygous state (genotype G/C) in your genome. This variant is located in the position 117243784 of chromosome 7 in an exonic region of the CFTR gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 952 the protein, causing a change from methionine to isoleucine (M952I).

rs121908748

The variant rs121908748 was detected in a heterozygous state (genotype G/A) in your genome. This variant is located in the position 117230494 of chromosome 7 in an exonic region of the CFTR gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function.

rs79660178

The variant rs79660178 was detected in a heterozygous state (genotype T/A) in your genome. This variant is located in the position 117171045 of chromosome 7 in an exonic region of the CFTR gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 122 the protein, causing a change from tyrosine to termination codon (Y122*).

rs75115087

The variant rs75115087 was detected in a heterozygous state (genotype A/T) in your genome. This variant is located in the position 117232349 of chromosome 7 in an exonic region of the CFTR gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 710 the protein, causing a change from lysine to termination codon (K710*).

rs397508536

The variant rs397508536 was detected in a heterozygous state (genotype A/T) in your genome. This variant is located in the position 117251799 of chromosome 7 in an exonic region of the CFTR gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 1102 the protein, causing a change from arginine to termination codon (R1102*).

rs77902683

The variant rs77902683 was detected in a heterozygous state (genotype G/C) in your genome. This variant is located in the position 117282622 of chromosome 7 in an exonic region of the CFTR gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function.

rs80055610

The variant rs80055610 was detected in a heterozygous state (genotype G/C) in your genome. This variant is located in the position 117227887 of chromosome 7 in an exonic region of the CFTR gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function.

rs397508453

The variant rs397508453 was detected in a heterozygous state (genotype G/C) in your genome. This variant is located in the position 117243836 of chromosome 7 in an exonic region of the CFTR gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 970 the protein, causing a change from glycine to arginine (G970R).

rs121909015

The variant rs121909015 was detected in a heterozygous state (genotype G/C) in your genome. This variant is located in the position 117282647 of chromosome 7 in an exonic region of the CFTR gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 1291 the protein, causing a change from glutamine to histidine (Q1291H).

rs121908748

The variant rs121908748 was detected in a heterozygous state (genotype G/C) in your genome. This variant is located in the position 117230494 of chromosome 7 in an exonic region of the CFTR gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function.

rs397508263

The variant rs397508263 was detected in a heterozygous state (genotype G/C) in your genome. This variant is located in the position 117227888 of chromosome 7 in an exonic region of the CFTR gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function.

rs121908763

The variant rs121908763 was detected in a heterozygous state (genotype C/G) in your genome. This variant is located in the position 117267694 of chromosome 7 in an exonic region of the CFTR gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 1196 the protein, causing a change from serine to termination codon (S1196*).

rs80034486

The variant rs80034486 was detected in a heterozygous state (genotype C/G) in your genome. This variant is located in the position 117292931 of chromosome 7 in an exonic region of the CFTR gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 1303 the protein, causing a change from asparagine to lysine (N1303K).

rs755416052

The variant rs755416052 was detected in a heterozygous state (genotype A/T) in your genome. This variant is located in the position 117254665 of chromosome 7 in an exonic region of the CFTR gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function.

rs149790377

The variant rs149790377 was detected in a heterozygous state (genotype T/A) in your genome. This variant is located in the position 117243667 of chromosome 7 in an exonic region of the CFTR gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 913 the protein, causing a change from tyrosine to termination codon (Y913*).

Characteristics and functions of the affected genes

CFTR

Cystic Fibrosis Transmembrane Conductance Regulator

The CFTR gene is encoded in chromosome 7. The CFTR gene encodes an epitelial ion and water transport channel. An ATP-binding cassette transporter (ABC) that functions as a low conductance selective channel gated by ATP hydrolysis. Exerts its function by modulating the activity of other ion channels and transporters. This protein functions as a channel across the membrane of cells that produce mucus, sweat, saliva, tears, and digestive enzymes. These channels are necessary for the normal function of organs such as the lungs and pancreas. More than 1,000 mutations in the CFTR gene have been identified in people with cystic fibrosis.

Other pathologies related to the variants found

Scientific reports have shown that the variant rs151048781 is associated with the occurrence of congenital bilateral absence of the vas deferens. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs121908748 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs79660178 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs75115087 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs397508536 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs77902683 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs80055610 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs397508453 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs121909015 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs121908748 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs397508263 is associated with the

occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs121908763 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs80034486 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs755416052 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs149790377 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Maple syrup urine disease

Maple syrup urine disease is an inherited disorder in which the body does not properly process certain protein building blocks. It is mainly characterized by the sweet, distinctive smell of the urine of the affected babies, vomiting, lack of energy and lethargy, abnormal movements and developmental delay. If left untreated, the maple syrup urine disease can cause seizures, coma and death. Maple syrup urine disease is classified by its pattern of signs and symptoms. The most common and serious form of the disease is the classic type, which becomes apparent soon after birth. The variant forms of the disorder occur in childhood and are usually milder, but if left untreated they can lead to developmental delay and other health problems.

Código 46 looks for pathogenic variants in your genome, these variants are directly related to the development of such disease. When the number of pathogenic variants detected is 0, it means that you do not have mutations that have already been clinically reported in patients who develop that disease. On the other hand, for some diseases, DRS is also calculated, which serves to compare a profile of variants with respect to populations, whether healthy or sick. Therefore, the number of pathogenic variants and the DRS are independent measurements.

BCKDHA	rs398123508	G/C	19	41928275	Heterozygous
BCKDHB	rs398124577	A/T	6	80878602	Heterozygous
BCKDHB	rs398124582	A/T	6	80878640	Heterozygous
BCKDHA	rs137852875	C/G	19	41928609	Heterozygous

Characteristics of the genetic variants detected

rs398123508

The variant rs398123508 was detected in a heterozygous state (genotype G/C) in your genome. This variant is located in the position 41928275 of chromosome 19 in an exonic region of the BCKDHA gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 285 the protein, causing a change from alanine to proline (A285P).

rs398124577

The variant rs398124577 was detected in a heterozygous state (genotype A/T) in your genome. This variant is located in the position 80878602 of chromosome 6 in an exonic region of the BCKDHB gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 163 the protein, causing a change from glutamic acid to valine (E163V).

rs398124582

The variant rs398124582 was detected in a heterozygous state (genotype A/T) in your genome. This variant is located in the position 80878640 of chromosome 6 in an exonic region of the BCKDHB gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 176 the protein, causing a change from asparagine to tyrosine (N176Y).

rs137852875

The variant rs137852875 was detected in a heterozygous state (genotype C/G) in your genome. This variant is located in the position 41928609 of chromosome 19 in an exonic region of the BCKDHA gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 310 the protein, causing a change from threonine to arginine (T310R).

Characteristics and functions of the affected genes

BCKDHA

2-oxoisovalerate dehydrogenase subunit alpha, mitochondrial

The BCKDHA gene is located in chromosome 19. The protein encoded by this gene is one part, the alpha subunit, of a group of enzymes called the branched-chain alpha-keto acid dehydrogenase (BCKD) enzyme complex. Two alpha subunits connect with two beta subunits, which are produced from the BCKDHB gene, to form a critical piece of the enzyme complex called the E1 component. The BCKD enzyme complex is responsible for one step in the normal breakdown of three amino acids: leucine, isoleucine, and valine. These amino acids are present in many kinds of food, particularly protein-rich foods such as milk, meat, and eggs. The BCKD enzyme complex is active in mitochondria, which serve as energy-producing centers. The breakdown of leucine, isoleucine, and valine produces molecules that can be used for energy. Mutations and deficiencies in this protein disrupt the normal function of the BCKD enzyme complex, preventing it from effectively breaking down leucine, isoleucine, and valine. As a result, these amino acids and their byproducts build up in the body. This accumulation is toxic to cells and tissues, particularly in the nervous system. Mutations and deficiencies of this gene are related to maple syrup urine disease.

BCKDHB

2-oxoisovalerate dehydrogenase subunit beta, mitochondrial

maple syrup urine disease

Other pathologies related to the variants found

Scientific reports have shown that the variant rs398123508 is associated with the occurrence of maple syrup urine disease. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs398124577 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs398124582 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs137852875 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Methylmalonic aciduria

Methylmalonic aciduria refers to a group of autosomal recessive diseases in which the body can not process the proteins and lipids of food, this can produce a lack of energy for the body and the accumulation of toxic substances in the blood. The symptoms of methylmalonic aciduria begin in infancy or early childhood with respiratory, eating, vomiting, weak muscle tone and lack of energy. A special diet for life and medical treatments are necessary to counteract the effects of the disease. If these symptoms are not treated, those affected can die at an early age. It has been seen that some people who have it present a moderate form of the disease that appears at the beginning of adult life.

Código 46 looks for pathogenic variants in your genome, these variants are directly related to the development of such disease. When the number of pathogenic variants detected is 0, it means that you do not have mutations that have already been clinically reported in patients who develop that disease. On the other hand, for some diseases, DRS is also calculated, which serves to compare a profile of variants with respect to populations, whether healthy or sick. Therefore, the number of pathogenic variants and the DRS are independent measurements.

Abstract	Pathogenic variants		Tested 24		Detected 3
Gene	Variant	Genotype	Chromosome	Position	Condition
MUT	rs121918255	C/G	6	49403186	Heterozygous
MUT	rs121918256	T/A	6	49425502	Heterozygous
SUCLG1	rs267607097	C/G	2	84670472	Heterozygous

Characteristics of the genetic variants detected

rs121918255

The variant rs121918255 was detected in a heterozygous state (genotype C/G) in your genome. This variant is located in the position 49403186 of chromosome 6 in an exonic region of the MUT gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 703 the protein, causing a change from glycine to arginine (G703R).

rs121918256

The variant rs121918256 was detected in a heterozygous state (genotype T/A) in your genome. This variant is located in the position 49425502 of chromosome 6 in an exonic region of the MUT gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 219 the protein, causing a change from asparagine to tyrosine (N219Y).

rs267607097

The variant rs267607097 was detected in a heterozygous state (genotype C/G) in your genome. This variant is located in the position 84670472 of chromosome 2 in an exonic region of the SUCLG1 gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 85 the protein, causing a change from glycine to alanine (G85A).

Characteristics and functions of the affected genes

MUT

Methylmalonyl-CoA mutase

The MUT gene is located on chromosome 6. The protein encoded by this gene is a mitochondrial enzyme called methylmalonyl-CoA mutase (MUT). This enzyme is involved in the degradation of amino acids, specifically; isoleucine, methionine, threonine and valine, certain types of lipids and cholesterol. To carry out the decomposition, the enzyme catalyses the molecules in methylmalonyl-CoA, subsequently and in conjunction with adenosylcobalamin (AdoCbI), catalyzes the isomerization of methylmalonyl-CoA to succinyl-CoA. Once succinyl-CoA is formed, other enzymes break it down into molecules that will then be used as energy. Mutations or deficiencies of the protein can cause mut-methylmalonic aciduria (MMAM), characterized by an often deadly disorder of the metabolism of organic acids. Common clinical features include lethargy, vomiting, growth retardation, hypotonia, neurological deficit and premature death.

SUCLG1

Succinate-CoA ligase alpha subunit

mitochondrial dna depletion syndrome 9 with or without methylmalonic aciduria

Other pathologies related to the variants found

Scientific reports have shown that the variant rs121918255 is associated with the occurrence of methylmalonic aciduria, mut(0) type. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs121918256 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Scientific reports have shown that the variant rs267607097 is associated with the occurrence of null. This disease is characterized by having autosomal recessive inheritance pattern.

Tyrosinemia

is a genetic disorder of autosomal recessive inheritance that affects the metabolism of the amino acid tyrosine. It is characterized by abnormally high levels of tyrosine in the blood (hypertirosinemia) and urine (tyrosinuria). It is divided into two forms; tyrosinemia type I and type II. Type I tyrosinemia is due to the deficiency of an enzyme called fumaratoacetoacetic hydrolase. It causes cirrhosis of the liver and without treatment, it leads to death due to liver failure. Other symptoms of this disease include diarrhea, bleeding in the stool, vomiting, swollen abdomen, slow weight gain, lethargy, irritability, yellow skin, bleeding, shortness of breath and mental retardation. Tyrosinemia type II is due to the deficiency of the enzyme tyrosine transaminase. It is characterized by the deposition of tyrosine crystals in the skin and eyes, areas of thickened skin (keratosis) on the palms of the hands and the soles of the feet, ulcers develop on the cornea and mental retardation. The treatment of thyrosemia requires drug treatment and a special diet for life. Children with the disease if treated early can have healthy growth and development.

Código 46 looks for pathogenic variants in your genome, these variants are directly related to the development of such disease. When the number of pathogenic variants detected is 0, it means that you do not have mutations that have already been clinically reported in patients who develop that disease. On the other hand, for some diseases, DRS is also calculated, which serves to compare a profile of variants with respect to populations, whether healthy or sick. Therefore, the number of pathogenic variants and the DRS are independent measurements.

Abstract	Pathogenic variants		Tested 5		Detected 1
Gene	**Variant**	**Genotype**	**Chromosome**	**Position**	**Condition**
FAH	rs121965073	A/T	15	80445443	Heterozygous

Characteristics of the genetic variants detected

rs121965073

The variant rs121965073 was detected in a heterozygous state (genotype A/T) in your genome. This variant is located in the position 80445443 of chromosome 15 in an exonic region of the FAH gene. It is known that the variant causes a change in the coding of the protein and this probably alters its folding and physiological function. The genetic mutation specifically alters the amino acid at position 16 the protein, causing a change from asparagine to isoleucine (N16I).

Characteristics and functions of the affected genes

FAH

Fumarylacetoacetase

The FAH gene is encoded on chromosome 15. The protein encoded by this gene is Fumarylacetoacetase. The FAH gene provides instructions for producing an enzyme called fumarateacetoacetate hydrolase. This enzyme is abundant in the liver, kidneys and there are smaller amounts that are found in many tissues throughout the body. Fumarylacetoacetate hydrolase is the latest in a series of five enzymes that work to break down the amino acid tyrosine. Specifically, fumarylacetoacetate hydrolase converts a by-product of tyrosine called acetoacetic fumarate into smaller molecules that are excreted by the kidneys or used to produce energy or produce other substances in the body. Several mutations of FAH can cause type I tyrosinemia. This condition is characterized by severe liver and kidney disease, neurological problems, and other signs and symptoms that begin in childhood. The altered FAH gene causing this condition produces an unstable or inactive enzyme, which results in reduced or absent fumarateacetoacetate hydrolase activity. The most common FAH mutation interrupts the way in which the instructions of the gene are used to produce the enzyme.

Other pathologies related to the variants found

Scientific reports have shown that the variant rs121965073 is associated with the occurrence of tyrosinemia type i. This disease is characterized by having autosomal recessive inheritance pattern.

HEALTH CONDITIONS FOR WHICH YOU DO NOT HAVE PATHOGENIC VARIANTS IN YOUR GENOME

Your genetic test included variants for which you have not shown pathogenic variants. Here the list of conditions for which you don't have variants:

- Alzheimer Disease
- Sickle cell anemia
- Breast cancer
- Hereditary breast and ovarian cancer
- Ovarian cancer
- Prosthate cancer
- Kidney carcinoma
- Cardiomyopaties
- Biotinidase deficiency
- Glucose 6 phosphate dehydrogenase deficiency
- 3 Methylcrotonyl-CoA carboxylase 1 deficiency
- Congenital adrenal hyperplasia
- Congenital hypothyroidism
- Parkinson Disease

Disease	Variants analyzed
3 Methylcrotonyl-CoA carboxylase 1 deficiency	rs119103213, rs185741664, rs544349961, rs727504005, rs727504006
Alzheimer's disease	rs63750082, rs63750687
Biotinidase deficiency	rs104893686, rs104893687, rs104893688, rs138818907, rs146015592, rs181396238, rs397514371, rs397514380, rs397514392, rs587783005, rs80338686
Breast cancer	rs397507384, rs398122661, rs72478580, rs730881468, rs786202461, rs786203754, rs80356888, rs80356913, rs80356936, rs80356937, rs80357063, rs80357233, rs80357295, rs80357463, rs80357475, rs80358721, rs80359175
Cardiomiopathy	rs121908990
Cystic fibrosis	rs113993959, rs121908748, rs121908749, rs121908750, rs121908751, rs121908752, rs121908754, rs121908755, rs121908760, rs121908763, rs121908764, rs121908765, rs121908791, rs121908792, rs121908793, rs121908794, rs121908797, rs121908803, rs121908810, rs121909011, rs121909012, rs121909015, rs121909017, rs121909019, rs121909025, rs121909026, rs121909036, rs121909045, rs121909047, rs139304906, rs139573311, rs141158996, rs143570767, rs149790377, rs151048781, rs193922503, rs201124247, rs267606722, rs368505753, rs372227120, rs374705585, rs374946172, rs387906362, rs387906369, rs397508168, rs397508173, rs397508176, rs397508200, rs397508201, rs397508211, rs397508227, rs397508243, rs397508247, rs397508249, rs397508263, rs397508267, rs397508279, rs397508296, rs397508328, rs397508331, rs397508336, rs397508350, rs397508378, rs397508387, rs397508393, rs397508394, rs397508435, rs397508442, rs397508453, rs397508464, rs397508470, rs397508532, rs397508536, rs397508538, rs397508596, rs397508604, rs397508675, rs397508684, rs397508701, rs397508702, rs397508746, rs397508759, rs397508761, rs397508778, rs397508796, rs397508799, rs74467662, rs74551128, rs74597325, rs74767530, rs75039782, rs75096551, rs75115087, rs75389940, rs75527207, rs755416052, rs75549581, rs75961395, rs76554633, rs76649725, rs76713772, rs77010898, rs77101217, rs77188391, rs77284892, rs77409459, rs77646904, rs77902683, rs78194216, rs78440224, rs78655421, rs78756941, rs78802634, rs79031340, rs79633941, rs79660178, rs797045160, rs79850223, rs80034486, rs80055610
Diabetes	rs104893879, rs104894331, rs104894338, rs114202595, rs121908540, rs121913148, rs121918671, rs121918673, rs121964990, rs1801483, rs193922335, rs193922338, rs28931580, rs28937891, rs28937892,

	rs74315374, rs77625743, rs794727236, rs797045209, rs80356669
Glucose 6 phosphate dehydrogenase deficiency	rs398123546, rs398123552, rs76723693, rs78365220
Hereditary breast and ovarian cancer	rs398122661, rs587780875, rs786202461, rs786203754, rs80356888, rs80356913, rs80356936, rs80356937, rs80357063, rs80357233, rs80357295, rs80357463, rs80357475, rs80358721, rs80359175
Kidney carcinoma	rs104893751
Maple syrup urine disease	rs121964988, rs121964990, rs121965004, rs137852871, rs137852874, rs137852875, rs182923857, rs371518124, rs375785084, rs398123490, rs398123491, rs398123496, rs398123497, rs398123503, rs398123508, rs398123509, rs398123513, rs398123660, rs398123665, rs398123669, rs398123674, rs398123675, rs398124561, rs398124574, rs398124577, rs398124582, rs398124589, rs398124592, rs398124593, rs398124602, rs794727262, rs794727635
Methylmalonic aciduria	rs104893851, rs121908538, rs121918251, rs121918252, rs121918254, rs121918255, rs121918256, rs121918257, rs138680796, rs140986055, rs201777056, rs267607097, rs28941784, rs369296618, rs387907119, rs398123276, rs398123278, rs398124434, rs564069299, rs571038432, rs727504020, rs727504022, rs756414548, rs760782399
Parkinson's disease	rs121908686, rs121908687, rs137853058, rs137853060, rs28940285, rs71799110, rs74315352, rs74315359
Prostate cancer	rs121908982, rs137852571, rs137852593, rs148960463
Tyrosinemia	rs121965073, rs370686447, rs80338894, rs80338895, rs80338901

TEST LIMITATIONS

The interpretation of the results of the tests carried out by Código 46 is limited by the information currently available. A more extensive interpretation may be possible in the future as more data and knowledge about human genetics and the health conditions accumulate.

When the genotyping does not reveal any difference with respect to the reference sequence, or when a variant is in a homozygous state, it cannot be certain that both alleles of an individual could be detected, this is a limitation of any platform of microarray genotyping.

Occasionally, an individual may carry an allele that is not amplified and detected due to a large deletion or insertion in its genome; in these cases, the marker can not be detected by our technology and therefore, this report does not contain information about this kind of alleles. Our tests do not detect copy number variants (CNV).

We evaluate single nucleotide variants (SNVs) in different coding exons for each gene included in our array. Unless specifically indicated, the report do not contain information on other genomic regions that have not been characterized. Unless otherwise indicated, the DNA sequence data is obtained from a specific cell type (from the sample of epithelial tissue collected by our kit). The results of this report do not contain information about the DNA sequence in other types of cells, tissues or organs. Because of this, our ability to detect variants due to somatic mosaicism is limited.

For this test we use the following reference genome (Genome build hg19, version GRCh37), a reinterpretation of your data under any other version of the human genome may differ from the results shown here.

We trust in our ability to track a sample once it has been received by Código 46. However, we are not responsible for any sample labeling error that occurs before the sample reaches Código 46.

These results should be used in the context of available clinical findings, and should not be used as the sole basis for treatment. This test was developed and its performance characteristics were determined by Código 46, which is certified under the ISO 9001: 2015 standard to perform highly complex clinical laboratory tests.

We recommend genetic counseling to help explain the results and analyze options for replication.

GLOSSARY

Allele
We have two copies of the same gene provided by each of our parents. An allele is the reference to each copy of the gene. That is, an individual inherits two alleles for each gene, one from the father and the other from the mother.

Autosomal Inheritance (Dominant or Recessive)
It is a pattern of inheritance in which the transmission of characteristics depends on the presence or absence of certain alleles. 'Autosomal' means that the gene in question is located on one of the non-sexual chromosomes (i.e., chromosome number 1 to 22). 'Dominant' means that a single copy of the mutation related to a disease is sufficient to cause the disease. On the contrary, a 'Recessive' character requires that both copies of the gene in question be altered, or mutated, in order for the disease to occur.

Chromosome
A chromosome is an ordered package of DNA found in the nucleus of the cell. Humans have 23 pairs of chromosomes - 22 autosomal pairs, and one pair of sex chromosomes, X and Y. Each parent contributes one chromosome of their pair so that the children get half of their chromosomes from their mother and half of their chromosomes from his father.

CNV
The copy number variation or CNV is when a section of the genome is repeated or absent. This is because the genome experiences gains and losses of genetic material.

DNA
The Deoxyribonucleic acid is a macromolecule that encodes the genes of cells, bacteria and some viruses. The DNA is the hereditary material of living beings and this information is used to make the proteins necessary for its development and functioning, as well as to regulate other functions of the organism. It is formed by a long sequence of nucleotides. Each nucleotide contains one of the 4 nitrogenous bases of DNA: adenine (A), thymine (T), cytosine (C) and guanine (G).

Exon
An exon is an element of the gene that contains the instructions for encoding amino acids.

Gene
The gene is the basic functional unit of inheritance. Genes are transmitted from parents to children and contain the necessary information to determine their traits. They are arranged in the chromosomes. Humans have approximately 20,000 genes organized into their chromosomes, representing ~ 1% of all the genetic information contained in each cell.

Genome
All the genetic information that is stored in the nucleus of each cell.

Genotype
A genotype is the collection of genes of an individual. The term can also refer to the two alleles inherited for a particular gene.

Genotyping / Genotyping
It is the procedure by which the genetic variants of an individual are determined. Their analysis allows to know the alleles that an individual has inherited from their biological parents.

Homozygous
If the two alleles are identical, i.e., when your genotype for the detected variant is identical in both copies of the gene.

Heterozygous
If the two alleles are different, i.e., your genotype for the detected variant is different in both copies of the gene.

Pathogenic variant
A genetic variant related with producing some type of disease.

Phenotype
The observable traits of an individual by the expression of the genotype, such as height, eye color, blood group and disease.

SNP
Single nucleotide polymorphisms are a type of change that occurs by a variation in a single DNA base pair. SNPs have been linked to health conditions, drug response and other phenotypes, this is what we explore and report in your genetic test.