INTRODUCTION

This document is your genetic report, which is a straightforward and non-technical presentation of the results from your Dante Labs Genetic Health Risk Test. The insights obtained from learning about your genes may enable you, in partnership with your healthcare provider, to formulate a plan to outsmart your genes and live a longer, more vibrant life. Our reports tell you how specific genetic variants in your DNA can affect your chances of developing certain health conditions. Genetic variants are differences in DNA between people. Some variants may increase the risk of developing certain health conditions. However, not everyone with a risk variant will develop these health conditions. For many of these conditions, people without a risk variant can also develop them. Some variants are more common in certain ethnicities. The effect a variant has on risk for a health condition is often best understood in those ethnicities. Since families share DNA, having a family history of a condition can increase risk. If you have a variant, your family members may also have that variant. For certain conditions, genetics is just one part of a person's total risk. You may be able to manage your risk for some conditions by managing other risk factors. Our tests do not diagnose any health conditions. Talk to your healthcare provider to better understand how to manage your risk. For more information, please visit our website at https://www.dantelabs.com/ and https://www.dantelabs.com/pages/faq

LIMITATIONS AND OTHER IMPORTANT INFORMATION

- This test provides genetic risk information based on assessment of specific genetic variants but does not report on your entire genetic profile. This test does not report all genetic variants related to a given disease or condition, and the absence of a variant tested does not rule out the presence of other genetic variants that may be related to the disease/condition.
- This test does not provide INDEL mutation analysis (INsertions/DELetions). Mutations analyzed include SNPs (Single Nucleotide Polymorphisms).
- Other genetic risk tests may report different genetic variants for the same disease/condition, so you may get different results using another genetic risk test.
- Other factors such as environmental and lifestyle risk factors may affect your risk of developing a given disease or health condition.
- This test is not a substitute for visits to your doctor or other health care professional. You should consult with your doctor or other health care professional if you have any questions or concerns about the results of your test or your current state of health.
- You may wish to speak to a genetic counselor, board-certified clinical molecular geneticist, or equivalent health care professional about the results of your test and to help answer any questions you may have. You can identify genetic counselors by visiting the National Society of Genetic Counselors website (https://www.nsgc.org).
- This test is not intended to diagnose any disease or condition, tell you anything about your current state of health, or be used to make medical decisions, including whether or not you should take a medication or how much of a medication you should take.
- The laboratory may not have been able to process your saliva sample. In this case Dante Labs will offer to send another kit to you to collect a second sample at no charge. If Dante Labs' attempts to process the second sample are unsuccessful, Dante Labs will not send additional sample collection kits and you or the person who paid for the Service (if that is not you) will be entitled to a complete refund of the amount paid to Dante Labs.
- For full Terms of Services, please visit: https://www.dantelabs.com/pages/terms-of-service
- This report has not been evaluated by the FDA. This product is not intended to diagnose, treat, cure, or prevent any disease

INFORMATION FOR HEALTH CARE PROFESSIONALS

- This test is not intended to diagnose a disease, determine medical treatment, or tell the user anything about their current state of health.
- This test is intended to provide users with their genetic information to inform lifestyle decisions and conversations with their doctor or other health care professional.
- Any diagnostic or treatment decisions should be based on testing and/or other information that you determine to be appropriate for your patient.

QUICK SUMMARY

NERVOUS SYSTEM DISORDERS

CONDITION NAME	RESULTS	MAIN MESSAGE
Parkinson Disease	✓	People with your genetic profile are likely to not have the predisposition for Parkinson disease.
Late-Onset Alzheimer's Disease	✓	People with your genetic profile are likely to not have a genetic predisposition for Alzheimer's Disease.

CANCER

CONDITION NAME	RESULTS	MAIN MESSAGE
Familial cancer of breast	✓	People with your genetic profile are likely not to have a genetic predisposition for Familial cancer of the breast.
Colorectal cancer, susceptibility	✓	People with your genetic profile are likely not to have a genetic predisposition for Colorectal cancer, susceptibility.
Prostate cancer	✓	People with your genetic profile are likely not to have a genetic predisposition for Prostate cancer.

CARDIAC CONDITIONS

CONDITION NAME	RESULTS	MAIN MESSAGE
Congenital long QT syndrome	✓	People with your genetic profile are likely not to have a genetic predisposition for Congenital long QT syndrome.

METABOLIC DISORDERS

CONDITION NAME	RESULTS	MAIN MESSAGE
Familial Hypercholesterolemia	✓	People with your genetic profile are likely to not have the predisposition for familial hypercholesterolemia.
Glucose 6 Phosphate Dehydrogenase Deficiency	✓	People with your genetic profile are likely to not have the predisposition for Glucose-6-phosphate dehydrogenase deficiency.
Celiac Disease	✓	People with your genetic profile are likely to not have the predisposition for Celiac disease
Insulin-resistance, susceptibility to	✓	People with your genetic profile are likely not to have a genetic predisposition for Insulin-resistance, susceptibility to.

RESPIRATORY DISEASES

CONDITION NAME	RESULTS	MAIN MESSAGE
Pulmonary Fibrosis	✓	People with your genetic profile are likely not to have a genetic predisposition for Pulmonary Fibrosis.

GASTROINTESTINAL TRACT DISORDERS

CONDITION NAME	RESULTS	MAIN MESSAGE
Hereditary pancreatitis	✓	People with your genetic profile are likely not to have a genetic predisposition for Hereditary pancreatitis.

BLOOD DISORDERS

CONDITION NAME	RESULTS	MAIN MESSAGE
Von Willebrand disease type 1	✓	People with your genetic profile are likely not to have a genetic predisposition for Von Willebrand disease type 1.
Hemochromatosis type 1	✓	People with your genetic profile are likely not to have a genetic predisposition for Hemochromatosis type 1.

SKIN DISORDERS

CONDITION NAME	RESULTS	MAIN MESSAGE

SKIN DISORDERS

CONDITION NAME	RESULTS	MAIN MESSAGE
Atopic dermatitis	✓	People with your genetic profile are likely not to have a genetic predisposition for Atopic dermatitis.

SYSTEMIC DISORDERS

CONDITION NAME	RESULTS	MAIN MESSAGE
Alpha-1 Antitrypsin Deficiency	✓	People with your genetic profile are likely to not have the predisposition for Alpha-1 antitrypsin deficiency.
Hereditary Amyloidosis (TTR-Related)	✓	People with your genetic profile are likely to not have the predisposition for Hereditary Transthyretin Amyloidosis.
SERPINA1-related Disorders	✓	People with your genetic profile are likely not to have a genetic predisposition for SERPINA1_related disorders.

ENDOCRINOLOGY DISORDERS

CONDITION NAME	RESULTS	MAIN MESSAGE
Obesity due to melanocortin 4 receptor deficiency	✓	People with your genetic profile are likely not to have a genetic predisposition for Obesity due to melanocortin 4 receptor deficiency.

ENDOTELIAL DISORDERS

CONDITION NAME	RESULTS	MAIN MESSAGE
Coronary artery disease	✓	People with your genetic profile are likely not to have a genetic predisposition for Coronary artery disease.

LIVER DISORDERS

CONDITION NAME	RESULTS	MAIN MESSAGE
Nonalcoholic Fatty Liver Disease	−	People with your genetic profile are likely to have a genetic predisposition for Nonalcoholic Fatty Liver Disease.

KEY SUMMARY

The above Summary provides an overview of the predicted risks for the patient. This information is based solely on genotype information and does not replace a doctor visit or a complete patient profile. Additionally, healthcare providers should consider family history, presenting symptoms, current prescriptions, and other factors before making any clinical or therapeutic decisions.

This colour means that you may not have negative associations based on genotype for the evaluated condition.

This colour means that you may have a variant potentially associated with an increased risk for the evaluated condition.

Parkinson Disease

RESULTS	
Parkinsonism is a clinical syndrome characterized by varying degrees of stiffness and various symptoms, including bradykinesia, tremor, and unstable posture, which can lead to profound gait impairment. Parkinsonism is characteristic of Parkinson's disease (PD). Symptoms like neurodegenerative diseases, specific brain injuries, head injuries, medications, and metabolic disorders, can be associated with other neurodegenerative diseases. Parkinson's disease (PD) is the most common cause of parkinsonism. It is a gradually progressive disease that manifests itself as asymmetric parkinsonism. Neuronal degeneration results in losing dopaminergic neurons in the midbrain and decreases dopamine levels. PD usually responds to levodopa therapy. Parkinsonism can sometimes be the first symptom of NPH. The first reports of Parkinson's and hydrocephalus features were related to posterior fossa tumours. **People with your genetic profile are likely to not have the predisposition for Parkinson disease.** According to the latest scientific discoveries, there is no documented genetic predisposition to Parkinson's disease in your results. Nevertheless, we recommend monitoring your health in accordance with your country's health recommendations and to check this finding again as we await the release of the new database from Clinvar.	
Publication 1 Publication 2 Publication 3 Publication 4	

Late-Onset Alzheimer's Disease

RESULTS	
Alzheimer's disease (AD) is the most common cause of cognitive decline. It is a neurodegenerative disease that usually affects people over the age of 65 and affects language, memory, comprehension, attention, judgment, and reasoning. The symptoms of Alzheimer's disease depend on the stage of the disease. Depending on the degree of cognitive impairment, Alzheimer's disease is divided into a preclinical or presymptomatic stage, a mild stage, and a demented stage. The first and most common symptom is episodic short-term memory loss. Impairment of short-term memory is followed by impairment of problem-solving ability, judgment, executive functions, lack of motivation, and disorganization leading to problems with multitasking and abstract thinking. Alzheimer's disease is an insidious and progressive neurodegenerative disease caused by the death of neurons. It typically begins in the entorhinal cortex in the hippocampus. Several risk factors are associated with Alzheimer's disease. Increasing age is the most important risk factor for the disease. Traumatic head injury, depression, cardiovascular and cerebrovascular disease, older age of parents, smoking, family history of dementia, elevated homocysteine levels, and the presence of the APOE e4 allele are known to increase the risk for Alzheimer's disease. **People with your genetic profile are likely to not have a genetic predisposition for Alzheimer's Disease.** According to the latest scientific discoveries, there is no documented genetic predisposition to Alzheimer's Disease. In your results. Nevertheless, we recommend monitoring your health in accordance with your country's health recommendations and to check this finding again as we await the release of the new database from Clinvar.	
Publication 1 Publication 2	

Familial Hypercholesterolemia

RESULTS	
Hypercholesterolemia is a condition characterized by very high levels of cholesterol in the blood. Cholesterol is a waxy fat-like substance produced in the body and comes from foods of animal origin (especially egg yolks, meat, poultry, fish and dairy products). The body needs this substance to build cell membranes, make certain hormones, and make compounds that help digest fats. People with hypercholesterolemia have a high risk of developing heart disease called coronary artery disease. This disease occurs when excess cholesterol in the bloodstream is deposited in the walls of blood vessels, particularly in the arteries that supply blood to the heart (coronary arteries). The abnormal accumulation of cholesterol forms lumps (plaque) that narrow and harden the walls of the arteries. The buildup of plaque in the coronary arteries causes a form of chest pain called angina and dramatically increases the risk of a heart attack. Hereditary forms of hypercholesterolemia can also cause health problems related to the accumulation of excess cholesterol in other tissues. **People with your genetic profile are likely to not have the predisposition for familial hypercholesterolemia.** According to the latest scientific discoveries, there is no documented genetic predisposition to familial hypercholesterolemia in your results. Nevertheless, we recommend monitoring your health in accordance with your country's health recommendations and to check this finding again as we await the release of the new database from Clinvar.	
Publication 1 Publication 2	

Insulin-resistance, susceptibility to

RESULTS	
Insulin resistance is a complex metabolic condition, considered the antechamber of type 2 diabetes. It is characterized by an altered sensitivity of cells to the action of insulin, one of the hormones produced by the pancreas, involved in the metabolism of sugars introduced with the diet. As a result of the normal release of insulin, glucose is introduced into cells and enters the metabolic pathways to be stored as an energy source. When the cells do not respond to the action of insulin, the pancreas reacts by producing more: this condition (known as hyperinsulinemia), if prolonged over time, tends to become chronic, also leading to a constant increase in blood sugar levels (the direct consequence of the altered signal of cellular utilization of sugars). Several factors can contribute to the development of insulin resistance: being overweight, having a sedentary lifestyle, smoking, hypercholesterolomy and hypertension are among the main ones. As previously mentioned, insulin resistance can progressively lead to the development of diabetes, passing through an intermediate condition called pre-diabetes. This exacerbation, however, is not mandatory: prediabetes, characterized by impaired fasting glycaemia and reduced glucose tolerance, can in fact be reversible in some cases; however, it is necessary to identify the underlying causes of these alterations and act on them. Genetic factors that can contribute to the development of insulin resistance include the IRS1 and ENPP1 genes, mutations of which represent risk factors for impaired cellular sensitivity to insulin. **People with your genetic profile are likely not to have a genetic predisposition for Insulin-resistance, susceptibility to.** Insulin resistance consists of a series of alterations in the glucose metabolism. Although it is closely related to the onset of type 2 diabetes, this exacerbation does not necessarily have to occur: it is in fact possible to act promptly to make insulin resistance controllable and / or reversible and increase cellular sensitivity to insulin. It is advisable to act on lifestyle habits: a healthy diet and regular physical exercise represent the first line strategy in controlling blood parameters related to glucose metabolism, and will also contribute to weight control (obesity is in fact one of the main risk factors for the onset of insulin resistance).	
Publication 1 Publication 2	

Glucose 6 Phosphate Dehydrogenase Deficiency

RESULTS	
(G6PD) Glucose-6-phosphate dehydrogenase is an enzyme present in the cytoplasm of all cells in the body. It is an enzyme that plays a vital role in preventing cell damage caused by reactive oxygen species (ROS). ROS are particularly dangerous for Erythrocytes due to their role in oxygen transport. The Gd gene encodes the G6PD enzyme. The Gd gene is found on the long arm of the X chromosome and is therefore subject to X-linked inheritance. For this reason, males are more commonly affected than females due to X-linked inheritance. In addition, G6PD deficiency may be due to mutations that alter the structure of the protein, reducing its activity or the amount of enzyme produced. Currently, 186 mutations are present in humans, most of which are point mutations affecting a single nucleotide. G6PD defect is the most common human enzyme alteration. affecting up to 400 million people worldwide. The disease is most prevalent in tropical and subtropical areas. Some studies state that G6PD deficiency protects against simple malaria but not severe malaria. In terms of ethnicity, G6PD deficiency is more common in people of African, Mediterranean, or Asian descent, possibly due to its purported protective effect against malaria. **People with your genetic profile are likely to not have the predisposition for Glucose-6-phosphate dehydrogenase deficiency.** According to the latest scientific discoveries, there is no documented genetic predisposition to Glucose-6-phosphate dehydrogenase deficiency in your results. Nevertheless, we recommend monitoring your health in accordance with your country's health recommendations and to check this finding again as we await the release of the new database from Clinvar.	
Publication 1 Publication 2	

Alpha-1 Antitrypsin Deficiency

RESULTS	
Alpha-1 antitrypsin deficiency can lead to lung and liver disease, an inherited disease. The signs of disease symptoms and the age at which they appear vary from person to person. Lung disease's first signs and symptoms usually appear between 20 and 50. The first symptoms are impaired exercise tolerance, shortness of breath after light activity, and wheezing. Unwanted weight loss, recurrent respiratory infections, fatigue, and a rapid heart rate on standing can be other disease symptoms. In addition, affected individuals often develop emphysema, a lung disease caused by damage to the small air sacs in the lungs (alveoli). Smoking or exposure to tobacco smoke accelerates the onset of emphysema and lung damage symptoms. About 10% of children with alpha-1 antitrypsin deficiency develop liver disease, including jaundice, which often causes yellowing of the skin and whites of the eyes. Adults with alpha-1 antitrypsin deficiency develop liver damage (cirrhosis) due to scar tissue formation in the liver. People with alpha-1 antitrypsin deficiency are also at risk of developing liver cancer called hepatocellular carcinoma. This condition is rare in people of Asian descent and affects 1 in 1,500 to 3,500 people of European descent. Some people with alpha-1 antitrypsin deficiency are misdiagnosed as having asthma. Mutations in the SERPIN1 gene cause alpha-1 antitrypsin deficiency. Mutations in the SERPIN1 gene can result in alpha-1 antitrypsin deficiency or an abnormal form of the protein that neutrophil elastase cannot control. Without sufficient functional alpha-1-antitrypsin, neutrophil elastase destroys the alveoli and causes lung disease. Abnormal alpha-1-antitrypsin can also build up in the liver and damage this organ. **People with your genetic profile are likely to not have the predisposition for Alpha-1 antitrypsin deficiency.** According to the latest scientific discoveries, there is no documented genetic predisposition to Alpha-1 antitrypsin deficiency in your results. Nevertheless, we recommend monitoring your health in accordance with your country's health recommendations and to check this finding again as we await the release of the new database from Clinvar.	
Publication 1 Publication 2	

Celiac Disease

RESULTS	
Celiac disease is an enteropathy of the small intestine. It is caused by exposure to gluten in the diet of susceptible individuals. The susceptibility is genetic. The disease is chronic and the only treatment currently is permanent exclusion of gluten from the diet. Patients with celiac disease may suffer from diarrhea and failure to thrive; some may be asymptomatic. The symptoms of celiac disease are due to damage to the enterocytes in the small intestine. In the full clinical picture, the typical features of the small intestine are chronic inflammation and villous atrophy. An individual must have the dominant HLA genes DQ2 or DQ8. The disease is the result of an adverse immune system response to gluten, and one of the main proteins involved is an antibody to tissue transglutaminase. However, there are other pathways that contribute to the disease. The glycoprotein gliadin (found in gluten) has a direct toxic effect on enterocytes by upregulating the production of IL -15. Some studies suggest that gastrointestinal infections in early childhood are important for the development of celiac disease later in life. This is not surprising given the organ involved, but it is likely that this is also directly related to the fact that celiac disease is caused by a disturbance in immune function. IgA antibodies to smooth muscle endomysium and tissue transglutaminase are commonly used to diagnose celiac disease. However, only about 5% of celiac patients are deficient in this immunoglobulin. A gluten-derived peptide called gliadin causes damage in the small intestine. Local inflammation occurs, and the process leads to destruction of the villi of the small intestine. This destruction, in turn, leads to decreased functionality of the intestinal surface and malabsorption. The lack of nutrient absorption directly affects the digestive system, but also indirectly affects all other systems of the body. This impact leads to overall poor health and is the reason celiac disease can have signs and symptoms that emanate from almost any system of the body, not just the gastrointestinal system. **People with your genetic profile are likely to not have the predisposition for Celiac disease** According to the latest scientific discoveries, there is no documented genetic predisposition to Celiac disease. In your results. Nevertheless, we recommend monitoring your health in accordance with your country's health recommendations and to check this finding again as we await the release of the new database from Clinvar.	
Publication 1 Publication 2	

Hereditary Amyloidosis (TTR-Related)

RESULTS	
Amyloidosis is an autosomal dominant inherited disease; this means that to develop the disease, an individual must inherit a copy of the affected gene from a parent. A genetic alteration that affects the function of a protein called transthyretin (TTR) cause HATTR amyloidosis. So far, 120 different mutations of the TTR gene are known. Symptoms of hATTR amyloidosis can vary widely between people carrying the same mutation and even within the same family. Therefore, different symptoms can appear at different times in each individual. The age at which the initial symptoms appear can range from 25 to 65 years. The TTR protein is mainly produced in the liver and is responsible for the transport of some proteins. Mutations in the gene that codes for the TTR protein cause changes in the shape of this protein. The misfolded proteins accumulate in the nervous system (nerves), the cardiovascular system (heart) and the gastrointestinal system (intestine), altering the function of organs. HATTR amyloidosis, which affects approximately 50,000 people worldwide, represents one of the primary unmet medical needs, with significant morbidity and mortality. Median survival is 4.7 years from diagnosis, with a reduced survival (3.4 years) for patients with cardiomyopathy. **People with your genetic profile are likely to not have the predisposition for Hereditary Transthyretin Amyloidosis.** According to the latest scientific discoveries, there is no documented genetic predisposition to Hereditary Transthyretin Amyloidosis in your results. Nevertheless, we recommend monitoring your health in accordance with your country's health recommendations and to check this finding again as we await the release of the new database from Clinvar.	
Publication 1 Publication 2	

SERPINA1-related Disorders

RESULTS	
The protein encoded by this gene is a serine protease inhibitor that belongs to the superfamily of serpins, whose targets include: elastase, plasmin, thrombin, trypsin, chymotrypsin and plasminogen activator. This protein is produced in the liver, bone marrow, lymphocytic and monocytic cells in lymphoid tissue, and Paneth cells in the intestine. Defects in this gene are associated with chronic obstructive pulmonary disease, emphysema, and chronic liver disease. Mutations in SERPINA1 are associated with alpha-1 antitrypsin deficiency (A1AT), which is inherited in an autosomal recessive manner. Clinical features of A1AT deficiency in the neonatal period are jaundice, pruritus, growth retardation, and hepatosplenomegaly. In adults, A1AT deficiency leads to lung disease. **People with your genetic profile are likely not to have a genetic predisposition for SERPINA1_related disorders.** According to the latest scientific discoveries, there is no documented genetic predisposition to SERPINA1_related Disorders. Nevertheless, we recommend monitoring your health in accordance with your country's health recommendations and to check this finding again as we await the release of the new database from Clinvar.	
Publication 1 Publication 2	

Pulmonary Fibrosis

RESULTS	
Idiopathic pulmonary fibrosis (IPF) is a chronic and progressive lung disease. This condition is associated with the formation of scar tissue (fibrosis) in the lungs leading to a progressive and irreversible decline in pulmonary function and ultimately respiratory failure. This disease usually affects people between the ages of 50 and 70. IPF belongs to a group of disorders called interstitial lung diseases (ILDs), which comprises a group of lung diseases involving inflammation or scarring of the lung tissue. Common signs and symptoms of IPF comprise shortness of breath and persistent dry, hacking cough. **People with your genetic profile are likely not to have a genetic predisposition for Pulmonary Fibrosis.** According to the latest scientific discoveries, there is no documented genetic predisposition to Pulmonary Fibrosis. Nevertheless, we recommend monitoring your health in accordance with your country's health recommendations and to check this finding again as we await the release of the new database from Clinvar.	
Publication 1 Publication 2	

Obesity due to melanocortin 4 receptor deficiency

RESULTS	
Melanocortin-4 receptor (MC4R) deficiency is the most common monogenetic form of obesity. However, the clinical spectrum and mode of inheritance are not defined, the pathophysiological mechanisms leading to obesity are poorly understood, and there is little information on the correlation between genotypeand phenotype. People with genetic mutations in MC4R (often referred to as MC4R deficiency) tend to gain weight in early childhood. People with MC4R deficiency have not only increased fat mass but also increased lean mass and increased linear growth in childhood. The increased growth may be due in part to disproportionate early hyperinsulinemia. The most important clinical feature in MC4R deficiency is hyperphagia, an increased urge to eat, and impaired satiety (less satiety after a meal). **People with your genetic profile are likely not to have a genetic predisposition for Obesity due to melanocortin 4 receptor deficiency.** According to the latest scientific discoveries, there is no documented genetic predisposition to Obesity due to melanocortin 4 receptor deficiency. Nevertheless, we recommend monitoring your health in accordance with your country's health recommendations and to check this finding again as we await the release of the new database from Clinvar.	
Publication 1 Publication 2	

Nonalcoholic Fatty Liver Disease

RESULTS

Nonalcoholic fatty liver disease (NAFLD) is a buildup of excess fat in the liver that can lead to liver damage similar to that caused by alcohol abuse but also occurs in people who do not drink much. The liver is a part of the digestive system that helps break down food, store energy, and remove waste products, including toxins. The liver usually contains some fat; it is called fatty liver (hepatic steatosis) when the liver contains more than 5 to 10 percent fat. The fatty deposits in the liver associated with NAFLD usually do not cause symptoms, although they can lead to elevated levels of liver enzymes that are detected in routine blood tests. Some affected individuals experience abdominal pain or fatigue. A physical examination may reveal mild enlargement of the liver. NAFLD most commonly occurs in middle-aged or elderly people, although younger people, including children, are also affected. It is often considered part of a group of conditions collectively known as metabolic syndrome.

People with your genetic profile are likely to have a genetic predisposition for Nonalcoholic Fatty Liver Disease.

The incidence and prevalence of non-alcoholic fatty liver disease (NAFLD) are rising and will continue to grow due to increasing obesity and lifestyle changes. Primary prevention with adequate management of metabolic derangement is essential to prevent the rising incidence of NAFLD and its associated complications. To lower the risk of heart disease, patients should be urged to reduce body weight, discontinue smoking, eat a healthy diet, and participate in regular exercise.

Publication 1 Publication 2

VARIANTS FOUND

Gene	rsID	Genotype
PNPLA3	rs738409	AG

Familial cancer of breast

RESULTS	
In familial breast cancer, family history is the main risk factor. Although the BRCA1 and BRCA2 genes are most commonly associated with the occurrence of familial forms of breast cancer, other mutations in other, albeit rarer, genes have been identified over time. ATM is one of them. This gene, normally involved in the development of ataxia telangiectasia, has been found in a mutated form in several families with familial breast cancer. RAD51, on the other hand, is a gene that interferes with recombination processes following double-stranded DNA breaks, and its loss of function leads to an increase in the mutation rate. This results in an accumulation of damage to the genetic material, which can lead to the onset of a carcinogenic process. This gene also interacts directly or indirectly with other genes involved in the development of familial forms of breast cancer, most notably BRCA1 and 2. **People with your genetic profile are likely not to have a genetic predisposition for Familial cancer of the breast.** According to the latest scientific evidence, you do not have a documented genetic predisposition to familial breast cancer. However, we recommend that you monitor your health according to your country's health recommendations and reassess this finding while we wait for the release of Clinvar's new database.	
Publication 1 Publication 2 Publication 3 Publication 4 Publication 5 Publication 6 Publication 7 Publication 8 Publication 9 Publication 10 Publication 11	

Colorectal cancer, susceptibility

RESULTS	
The most common cancer in men and women is Colorectal cancer. It represents the second leading cause of all the cancer-related deaths in the United States, with 151,030 estimated new cases and 52,580 estimated deaths in 2022. Most colorectal cancer cases occur sporadically, suggesting a role for de novo mutations. However, inherited mutations or cancer syndromes cause about 5% to 10% of cases. Hereditary Non-Polyposis Colorectal Cancer Syndrome (HNPCC) represents the most common inherited form of colorectal cancer. Therefore, identifying patients with Lynch syndrome is clinically relevant because the lifetime risk of colorectal cancer in people with this condition critically increases up to 80%. In addition, an increased risk of other primary cancers are observed (e.g. gastric, ovarian, small bowel, urothelial, biliary and pancreatic cancer, glioblastoma, sebaceous gland adenomas, and keratoacanthomas). **People with your genetic profile are likely not to have a genetic predisposition for Colorectal cancer, susceptibility.** According to the latest scientific evidence, there is no documented genetic predisposition to colorectal cancer in your results. However, we recommend that you monitor your health according to your country's health recommendations and review this result while we wait for the release of Clinvar's new database.	
Publication 1 Publication 2	

Prostate cancer

RESULTS	
Prostate cancer is a common form of cancer that affects men, usually middle-aged. In its early stages, it may not give any symptoms and the diagnosis can therefore occur as a random finding in the prevention and screening programs, by measuring some specific blood parameters (PSA) or physical examinations such as the digital rectal exam. Some typical signs and symptoms may occur with the growth of the tumor mass, such as impaired urinary flow, a feeling of incomplete bladder emptying, presence of blood in the urine and semen, or pain during ejaculation. This symptomatology, however, is not necessarily due to the presence of a tumor, as it is also found in other non-neoplastic conditions. Although the majority of prostate cancers are sporadic, a small percentage are hereditary; this form tends to develop earlier and is linked to several genes, including HOXB13. Genetic factors that can increase susceptibility to prostate cancer include the CHEK2 gene, which is considered a multi-organ cancer susceptibility gene, among others. This gene is a tumor suppressor that regulates cell proliferation and is involved in DNA damage checkpoints. Mutations in this gene can therefore lead cells to aberrant proliferation phenomena. **People with your genetic profile are likely not to have a genetic predisposition for Prostate cancer.** The onset of prostate cancer is the result of many factors including genetic predisposition, which plays an important role in this and all other forms of cancer. Age is also an important risk factor: the risk of getting sick, in fact, increases after the age of 50. Not to be overlooked is also familiarity and eating habits: it has in fact been shown in numerous studies that a diet rich in fat can contribute to the development of this pathology. It is therefore important to follow a healthy lifestyle, avoiding or at least limiting the intake of foods rich in saturated fats and favoring fresh foods such as fruit and vegetables and whole grains. Prevention is implemented by undergoing an annual urological examination with a PSA dosage, if you are over 50 years old and / or have a family history for this neoplasm.	
Publication 1 Publication 2 Publication 3	

Congenital long QT syndrome

RESULTS	
Long QT syndrome (LQTS) is characterized by QT prolongation and T-wave abnormalities on the ECG associated with tachyarrhythmias, typically ventricular tachycardia, and torsade de Pointes (TdP). TdP usually ends independently and causes syncope, the most common symptom in individuals with LQTS. Syncope usually occurs precipitously and without warning. In some cases, TdP progresses to ventricular fibrillation and cardiac arrest or sudden death. Approximately 50% or fewer untreated individuals with a pathogenic variant in one of the 15 genes associated with LQTS have symptoms. The number of syncopal events in symptomatic individuals ranges from one to hundreds, with an average of only a few. Most common phenotypes: Pathogenic variants in KCNH2, KCNQ1, and SCN5A account for most LQTS cases, and significant genotype-phenotype correlations have been reported. Three clinical phenotypes (LQTS types 1, 2, and 3) have been reported in individuals with pathogenic variants in these genes. The QTc range is similar in all phenotypes (~400-600+ msec). Mean QTc values are similar for LQTS type 1 and LQTS type 2 phenotypes and slightly longer for the LQTS type 3 phenotype. Characteristic T-wave patterns have been reported for LQTS phenotypes types 1, 2, and 3, which may be helpful in molecular genetic testing strategies to identify the gene involved. Cardiac events often have genotype-specific triggers. In LQTS phenotype 1, symptoms are most commonly triggered by physical exertion, whereas in LQTS phenotype 2, events are most commonly triggered by auditory stimuli and emotional stress. In LQTS phenotype 3, symptoms occur mainly during sleep. **People with your genetic profile are likely not to have a genetic predisposition for Congenital long QT syndrome.** According to the latest scientific discoveries, there is no documented genetic predisposition to Long QT Syndrome in your results. Nevertheless, we recommend monitoring your health in accordance with your country's health recommendations and to check this finding again as we await the release of the new database from Clinvar.	
Publication 1 Publication 2 Publication 3 Publication 4 Publication 5 Publication 6 Publication 7 Publication 8 Publication 9	

Von Willebrand disease type 1

RESULTS	
Von Willebrand Disease (VWD) type 1 is an inherited bleeding disorder and the most common form of VWD. This disease is characterized by partial quantitative deficiency of von Willebrand factor (VWF levels < 50 IU/dL). VWF is a multimeric plasma protein crucial for platelet adhesion to the subendothelium of injured vessel walls and for binding and stabilizing the coagulation factor VII in the blood. Therefore, predominant symptoms are associated with mucosal bleeding, including heavy menstrual bleeding and persistent oozing after trauma or surgery. **People with your genetic profile are likely not to have a genetic predisposition for Von Willebrand disease type 1.** According to the latest scientific discoveries, there is no documented genetic predisposition to Von Willebrand disease in your results. Nevertheless, we recommend monitoring your health in accordance with your country's health recommendations and to check this finding again as we await the release of the new database from Clinvar.	
Publication 1 Publication 2 Publication 3 Publication 4 Publication 5	

Hemochromatosis type 1

RESULTS	
Hereditary hemochromatosis is when the body absorbs too much iron from food. As a result, excess iron is stored in the tissues and organs of the body, particularly in the skin, heart, liver, pancreas and joints. Excess iron can overload and eventually damage tissues and organs because the body cannot release it. For this reason, hereditary hemochromatosis is also known as an iron overload disorder. Early symptoms of hereditary hemochromatosis are non-specific and can include fatigue, joint pain, and abdominal pain. Environment and lifestyle factors such as the amount of iron in the diet, alcohol consumption, and infections influence the onset and progression of symptoms. Hereditary hemochromatosis is classified into different types depending on the age of onset and other factors such as the genetic cause and the mode of inheritance. **People with your genetic profile are likely not to have a genetic predisposition for Hemochromatosis type 1.** According to the latest scientific discoveries, there is no documented genetic predisposition to Hereditary Hemochromatosis in your results. Nevertheless, we recommend monitoring your health in accordance with your country's health recommendations and to check this finding again as we await the release of the new database from Clinvar.	
Publication 1 Publication 2 Publication 3 Publication 4	

Atopic dermatitis

RESULTS	
Atopic dermatitis (AD), a specific form of eczema, is the most common chronic inflammatory skin disease. The disease usually begins in early childhood and often disappears before puberty. However, in some sufferers, the disease continues into adulthood, and in others, it does not begin until adulthood. Hallmarks of atopic dermatitis are dry, itchy skin and red rashes that come and go. The rashes can occur on any part of the body, and the pattern varies at different ages. Atopic dermatitis has a complex etiology that includes genetic and environmental factors that lead to abnormalities of the epidermis and immune system. **People with your genetic profile are likely not to have a genetic predisposition for Atopic dermatitis.** According to the latest scientific discoveries, there is no documented genetic predisposition to atopic dermatitis in your results. Nevertheless, we recommend monitoring your health in accordance with your country's health recommendations and to check this finding again as we await the release of the new database from Clinvar.	
Publication 1 Publication 2 Publication 3 Publication 4	

Coronary artery disease

RESULTS	
Coronary artery disease results from the narrowing of the coronary arteries due to fatty deposits on the inner wall of the artery. This narrowing reduces blood flow and increases the chances of a clot forming, blocking the artery, which can cause a heart attack. This condition is responsible for about one-third of all deaths worldwide in people over 35. Arteries narrow when plaque, made up of fat, cholesterol, and other blood substances, begins to build up in the artery walls. This hardens the arteries, causing them to not respond adequately to cardiac stress. As a result, the heart cannot get the oxygen-rich blood it needs. Symptoms, such as shortness of breath and chest pain (angina pectoris), can occur during exercise, emotional stress, or even at rest. As plaque develops, it can completely block the artery, preventing part of the heart muscle from receiving oxygen and causing a heart attack. As a result, the vessels are often blocked or constricted in several places. A blocked brain artery can lead to stroke. When arteries outside the heart are affected, the disease is called peripheral artery disease (PAD). The triggers are uncontrolled hypertension, diabetes, smoking and some genetic factors. After the initial insult, the endothelium releases inflammatory cytokines and becomes highly receptive to leukocytes, particularly monocytes and platelets. Monocytes attracted to the endothelium mature to become macrophages and engulf oxidized LDL particles to form foamy lipid-laden macrophages. Due to continued inflammation, there is also migration and proliferation of smooth muscle, which eventually forms a fibrous plaque. **People with your genetic profile are likely not to have a genetic predisposition for Coronary artery disease.** According to the latest scientific discoveries, there is no documented genetic predisposition to Coronary artery disease in your results. Nevertheless, we recommend monitoring your health in accordance with your country's health recommendations and to check this finding again as we await the release of the new database from Clinvar.	
Publication 1 Publication 2 Publication 3 Publication 4 Publication 5 Publication 6 Publication 7 Publication 8 Publication 9	

Hereditary pancreatitis

RESULTS	
Hereditary pancreatitis involves the onset of multiple inflammatory episodes affecting this organ, which manifest themselves with abdominal pain, nausea and vomiting. The onset is in infancy and, due to the persistent inflammatory state, subjects affected by this condition may suffer from chronic pancreatitis, presenting a series of symptoms that include weight loss (due to the malabsorption of nutrients present in food) and fatty stools. The attention to possible mutations in the SPINK1 gene in the pathogenesis of hereditary pancreatitis derives from the observation that, in many cases, there were no mutations in the most involved gene, PRSS1. SPINK1 encodes a secretory trypsin inhibitor, having a protective function against the recurrent activation of trypsin (a digestive protease). Its mutations, therefore, involve an imbalance of the protease/antiprotease system, exposing the pancreas to a pro-inflammatory environment capable of leading to pancreatitis. **People with your genetic profile are likely not to have a genetic predisposition for Hereditary pancreatitis.** According to the latest scientific discoveries, there is no documented genetic predisposition to hereditary pancreatitis in your results. Nevertheless, we recommend monitoring your health in accordance with your country's health recommendations and to check this finding again as we await the release of the new database from Clinvar.	
Publication 1 Publication 2 Publication 3 Publication 4 Publication 5 Publication 6	

GLOSSARY

ALLELE	An allele is a variant form of a gene that is located at a specific position (or genetic locus) on a specific chromosome. Humans have two alleles at each genetic locus, with one allele inherited from each parent.
CHROMOSOME	A chromosome is a condensed thread-like structure of DNA that carries hereditary information, or genes. Human cells have 22 chromosome pairs plus two sex chromosomes with a total of 46 per cell.
GENOME	A genome is an organisms'complete set of DNA, including all of its genes. Each genome contains all the information needed to build and maintain that organism. In humans, a copy of the entire genome—more than 3 billion DNA base pairs—is contained in all cells that have a nucleus.
GENOTYPE	A genotype is the genetic makeup of an individual organism. It may also refer to just a particular gene or set of genes carried by an individual. The genotype determines the phenotype, or observable traits of the organism.
ODDS RATIO	The odds ratio is a way of comparing whether the odds of a certain outcome is the same for two different groups. In this report, the odds ratio estimates the probability of a condition occurring in a group of people with a certain genetic variant compared to a group of people without that same variant. An odds ratio of 1 means that the two groups are equally likely to develop the condition. An odds ratio higher than 1 means that the people with the genetic variant are more likely to develop the condition, while an odds ratio of less than1 means that people with the variant are less likely to develop the condition.
PHENOTYPE	Phenotype is a description of an individuals'physical characteristics, including appearance, development and behavior. The phenotype is determined by the individual's genotype as well as environmental factors.
POPULATION ALLELE FREQUENCY	The allele frequency represents the incidence of a variant in a population. Alleles are variant forms of a gene that are located at the same position, or genetic locus, on a chromosome.
SNP	Single nucleotide polymorphisms, frequently called SNPs, are the most common type of genetic variation among people. A SNP is a variation in a single nucleotide that occurs at a specific position in the genome.