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DANTE LABS™ TEST RESULTS

KIT ID: 60820188474029

INTRODUCTION

This document is your genetic report, which is a straightforward and non-technical presentation of the results. It provides clear solutions to optimize your health and longevity. The insights obtained from learning about your genes may enable you, in partnership with your healthcare provider, formulate a plan to outsmart your genes and live a longer, more vibrant life. Our reports tell you how your DNA can affect your chances of developing certain health conditions. Genetic variants are differences inDNA 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 studied 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.

QUICK SUMMARY

NERVOUS SYSTEM DISORDERS		
CONDITION NAME	RESULTS	MAIN MESSAGE
Neurofibromatosis type 2	✓	No variants detected
Canavan disease	✓	No variants detected
D-bifunctional protein deficiency	✓	No variants detected
Familial dysautonomia	✓	No variants detected
Leigh syndrome	✓	No variants detected
Neuronal Ceroid Lipofuscinosis CLN1 Related	✓	No variants detected
Neuronal Ceroid Lipofuscinosis CLN5 Related	✓	No variants detected
Sialic acid storage disease	✓	No variants detected
Tay-Sachs disease	✓	No variants detected
CANCER		
CONDITION NAME	RESULTS	MAIN MESSAGE
Familial adenomatous polyposis	✓	No variants detected
Li-Fraumeni syndrome	✓	No variants detected
Peutz-Jeghers syndrome	✓	No variants detected
Pilomatrixoma	✓	No variants detected
PTEN Hamartoma Tumor Syndrome	✓	No variants detected
Paragangliomas	✓	No variants detected
Tuberous sclerosis	✓	No variants detected
Von Hippel-Lindau syndrome	✓	No variants detected
NEUROMUSCULAR DISORDERS		

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NEUROMUSCULAR DISORDERS

CONDITION NAME	RESULTS	MAIN MESSAGE
Andermann syndrome	✓	No variants detected
Limb-girdle muscular dystrophy	✓	No variants detected

RENAL DISORDERS

CONDITION NAME	RESULTS	MAIN MESSAGE
Polycystic kidney disease	✓	No variants detected
Primary hyperoxaluria	✓	No variants detected

CARDIAC CONDITIONS

CONDITION NAME	RESULTS	MAIN MESSAGE
Arrhythmogenic right ventricular cardiomyopathy	✓	No variants detected
Catecholaminergic polymorphic ventricular tachycardia	✓	No variants detected
Familial thoracic aortic aneurysm and dissection	✓	No variants detected
Brugada syndrome	✓	No variants detected
Dilated Cardiomyopathy	✓	No variants detected
Familial hypertrophic cardiomyopathy	✓	No variants detected
Left ventricular noncompaction	✓	No variants detected
Long QT Syndrome	✓	No variants detected

CONNECTIVE TISSUE DISORDER

CONDITION NAME	RESULTS	MAIN MESSAGE
Ehlers-Danlos syndrome	✓	No variants detected
Loeys-Dietz syndrome	✓	No variants detected
Marfan syndrome	✓	No variants detected
Rhizomelic chondrodysplasia punctata	✓	No variants detected

BONE MARROW DISEASES

CONDITION NAME	RESULTS	MAIN MESSAGE
Fanconi anemia	✓	No variants detected

METABOLIC DISORDERS

CONDITION NAME	RESULTS	MAIN MESSAGE
Fabry disease	✓	No variants detected
Familial Hypercholesterolemia	✓	No variants detected
Ornithine transcarbamylase deficiency	✓	No variants detected
Wilson Disease	✓	No variants detected
PMM2-congenital disorder of glycosylation	✓	No variants detected
Dihydrolipoamide dehydrogenase deficiency	✓	No variants detected
Familial Hyperinsulinism	✓	No variants detected

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METABOLIC DISORDERS

CONDITION NAME	RESULTS	MAIN MESSAGE
Gaucher disease	✓	No variants detected
Glycogen storage disease type I	✓	No variants detected
GRACILE syndrome	✓	No variants detected
Hereditary fructose intolerance	✓	No variants detected
Maple syrup urine disease	✓	No variants detected
Medium-Chain Acyl-Coenzyme A Dehydrogenase Deficiency	✓	No variants detected
Mucolipidosis type IV	✓	No variants detected
Niemann-Pick Disease Type A	✓	No variants detected
Phenylketonuria	✓	No variants detected
Tyrosinemia	✓	No variants detected
Hereditary Hemochromatosis	✓	No variants detected
Glucose-6-phosphate dehydrogenase deficiency	✓	No variants detected

RESPIRATORY DISEASES

CONDITION NAME	RESULTS	MAIN MESSAGE
Cystic fibrosis	✓	No variants detected

GASTROINTESTINAL TRACT DISORDERS

CONDITION NAME	RESULTS	MAIN MESSAGE
Juvenile polyposis syndrome	✓	No variants detected

BLOOD DISORDERS

CONDITION NAME	RESULTS	MAIN MESSAGE
Beta thalassemia	✓	No variants detected
Sickle cell disease	✓	No variants detected
Factor V Leiden thrombophilia	✓	No variants detected
Prothrombin thrombophilia	✓	No variants detected

SKIN DISORDERS

CONDITION NAME	RESULTS	MAIN MESSAGE
Bloom syndrome	✓	No variants detected
Junctional epidermolysis bullosa	✓	No variants detected
Sjögren-Larsson syndrome	✓	No variants detected

SENSORIAL DISORDERS

CONDITION NAME	RESULTS	MAIN MESSAGE
Nonsyndromic Hearing Loss and Deafness GJB2 Related	✓	No variants detected
Pendred syndrome	✓	No variants detected
Usher Syndrome Type I	✓	No variants detected
Age-related macular degeneration	⛔	We have found a variant associated with Age-related macular degeneration

SYSTEMIC DISORDERS		
CONDITION NAME	RESULTS	MAIN MESSAGE
Nijmegen breakage syndrome	✓	No variants detected
Zellweger spectrum disorder	✓	No variants detected
Alpha-1 antitrypsin deficiency	✓	No variants detected

DRUG RESPONSE		
CONDITION NAME	RESULTS	MAIN MESSAGE
Malignant hyperthermia	✓	No variants detected

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. Healthcare providers should consider also family history, presenting symptoms, current prescriptions,

and other factors before making any clinical or therapeutic decisions.

No negative assertions based on genotype; no increased risk for the evaluated condition.

We have found a variant associated with an increased risk for this condition.

DETAILED INFORMATION

AGE-RELATED MACULAR DEGENERATION

Variant found:

- **Gene: CFH**
- **Marker: rs1061170**
- **Position: chr1:196659237**

We have found a heterozygous variant associated with Age-related macular degeneration in the CFH gene.

Your genetic make up evidences a nucleotide change from a T to a C in the DNA. This variant is present on one copy of chromosome 1 in position 196659237.

We have found a variant associated with Age-related macular degeneration

Description

Age-related macular degeneration is an eye disease that is a leading cause of vision loss in older people in developed countries. The vision loss usually becomes noticeable in a person's sixties or seventies and tends to worsen over time.

Age-related macular degenerationmainly affects central vision, which is needed for detailed tasks such as reading, driving, and recognizing faces. The vision loss in this condition results from a gradual deterioration of light-sensing cells in the tissue at the back of the eye that detects light and color (the retina). Specifically, age-related macular degeneration affects a small area near the center of the retina, called the macula, which is responsible for central vision. Side (peripheral) vision and night vision are generally not affected, but reduced dim light (scotopic) vision often occurs in the early stages of the disease.

Researchers have described two major types of age-related macular degeneration, known as the dry form and the wet form. The dry form is much more common, accounting for 85 to 90 percent of all cases of age-related macular degeneration. It is characterized by a buildup of yellowish deposits called drusen beneath the retina and vision loss that worsens slowly over time. The condition typically affects vision in both eyes, although vision loss often occurs in one eye before the other.

The wet form of age-related macular degeneration is associated with severe vision loss that can worsen rapidly. This form of the condition is characterized by the growth of abnormal, fragile blood vessels underneath the macula. These vessels leak blood and fluid, which damages the macula and makes central vision appear blurry and distorted.

Frequency

Age-related macular degeneration has an estimated prevalence of 1 in 2,000 people in the United States and other developed countries. The condition currently affects several million Americans, and the prevalence is expected to increase over the coming decades as the proportion of older people in the population increases.

For reasons that are unclear, age-related macular degeneration affects individuals of European descent more frequently than African Americans in the United States.

Causes

Age-related macular degeneration results from a combination of genetic and environmental factors. Many of these factors have been identified, but some remain unknown.

Researchers have considered changes in many genes as possible risk factors for age-related macular degeneration. The best-studied of these genes are involved in a part of the body's immune response known as the complement system. This system is a group of proteins that work together to destroy foreign invaders (such as bacteria and viruses), trigger inflammation, and remove debris from cells and tissues. Genetic changes in and around several complement system genes, including the CFH gene, contribute to a person's risk of developing age-related macular degeneration. It is unclear how these genetic changes are related to the retinal damage and vision loss characteristic of this condition.

Changes on the long (q) arm of chromosome 10 in a region known as 10q26 are also associated with an increased risk of age-related macular degeneration. The 10q26 region contains two genes of interest, ARMS2 and HTRA1. Changes in both genes have been studied as possible risk factors for the disease. However, because the two genes are so close together, it is difficult to tell which gene is associated with age-related macular degeneration risk, or whether increased risk results from variations in both genes.

Other genes that are associated with age-related macular degeneration include genes involved in transporting and processing high-density lipoprotein (HDL, also known as "good" cholesterol) and genes that have been associated with other forms of macular disease.

Researchers have also examined nongenetic factors that contribute to the risk of age-related macular degeneration. Age appears to be the most important risk factor; the chance of developing the condition increases significantly as a person gets older. Smoking is another established risk factor for age-related macular degeneration. Other factors that may increase the risk of this condition include high blood pressure, heart disease, a high-fat diet or one that is low in certain nutrients (such as antioxidants and zinc), obesity, and exposure to ultraviolet (UV) rays from sunlight. However, studies of these factors in age-related macular degeneration have had conflicting results

Actions and Advice

Who is at risk?

Age is a major risk factor for AMD. The disease is most likely to occur after age 60, but it can occur earlier. Other risk factors for AMD include:

- **Smoking**. Research shows that smoking doubles the risk of AMD.
- **Race**. AMD is more common among Caucasians than among African-Americans or Hispanics/Latinos.
- **Family history and Genetics**. People with a family history of AMD are at higher risk. At last count, researchers had identified nearly 20 genes that can affect the risk of developing AMD. Many more genetic risk factors are suspected. You may see offers for genetic testing for AMD. Because AMD is influenced by so many genes plus environmental factors such as smoking and nutrition, there are currently no genetic tests that can diagnose AMD, or predict with certainty who will develop it. The American Academy of Ophthalmology currently recommends against routine genetic testing for AMD, and insurance generally does not cover such testing.

Does lifestyle make a difference?

Researchers have found links between AMD and some lifestyle choices, such as smoking. You might be able to reduce your risk of AMD or slow its progression by making these healthy choices:

- Avoid smoking
- Exercise regularly
- Maintain normal blood pressure and cholesterol levels
- Eat a healthy diet rich in green, leafy vegetables and fish

How is AMD detected?

The early and intermediate stages of AMD usually start without symptoms. Only a comprehensive dilated eye exam can detect AMD. The eye exam may include the following:

- **Visual acuity test.** This eye chart measures how well you see at distances.
- **Dilated eye exam.** Your eye care professional places drops in your eyes to widen or dilate the pupils. This provides a better view of the back of your eye. Using a special magnifying lens, he or she then looks at your retina and optic nerve for signs of AMD and other eye problems.
- **Amsler grid.** Your eye care professional also may ask you to look at an Amsler grid. Changes in your central vision may cause the lines in the grid to disappear or appear wavy, a sign of AMD.
- **Fluorescein angiogram.** In this test, which is performed by an ophthalmologist, a fluorescent dye is injected into your arm. Pictures are taken as the dye passes through the blood vessels in your eye. This makes it possible to see leaking blood vessels, which occur in a severe, rapidly progressive type of AMD (see below). In rare cases, complications to the injection can arise, from nausea to more severe allergic reactions.
- **Optical coherence tomography.** You have probably heard of ultrasound, which uses sound waves to capture images of living tissues. OCT is similar except that it uses light waves, and can achieve very high-resolution images of any tissues that can be penetrated by light—such as the eyes. After your eyes are dilated, youll be asked to place your head on a chin rest and hold still for several seconds while the images are obtained. The light beam is painless.

During the exam, your eye care professional will look for *drusen*, which are yellow deposits beneath the retina. Most people develop some very small drusen as a normal part of aging. The presence of medium-to-large drusen may indicate that you have AMD.

Another sign of AMD is the appearance of pigmentary changes under the retina. In addition to the pigmented cells in the iris (the colored part of the eye), there are pigmented cells beneath the retina. As these cells break down and release their pigment, your eye care professional may see dark clumps of released pigment and later, areas that are less pigmented. These changes will not affect your eye color.

Questions to ask your eye care Professional

Below are a few questions you may want to ask your eye care professional to help you understand your diagnosis and treatment. If you do not understand your eye care professional's responses, ask questions until you do understand.

- What is my diagnosis and how do you spell the name of the condition?
- Can my AMD be treated?
- How will this condition affect my vision now and in the future?
- What symptoms should I watch for and how should I notify you if they occur?
- Should I make lifestyle changes?

What are the stages of AMD?

There are three stages of AMD defined in part by the size and number of drusen under the retina. It is possible to have AMD in one eye only, or to have one eye with a later stage of AMD than the other.

- **Early AMD.** Early AMD is diagnosed by the presence of medium-sized drusen, which are about the width of an average human hair. People with early AMD typically do not have vision loss.
- **Intermediate AMD.** People with intermediate AMD typically have large drusen, pigment changes in the retina, or both. Again, these changes can only be detected during an eye exam. Intermediate AMD may cause some vision loss, but most people will not experience any symptoms.
- **Late AMD.** In addition to drusen, people with late AMD have vision loss from damage to the macula. There are two types of late AMD:
  - In geographic atrophy (also called dry AMD), there is a gradual breakdown of the light-sensitive cells in the macula that convey visual information to the brain, and of the supporting tissue beneath the macula. These changes cause vision loss.

- In neovascular AMD (also called wet AMD), abnormal blood vessels grow underneath the retina. ("Neovascular" literally means "new vessels.") These vessels can leak fluid and blood, which may lead to swelling and damage of the macula. The damage may be rapid and severe, unlike the more gradual course of geographic atrophy. It is possible to have both geographic atrophy and neovascular AMD in the same eye, and either condition can appear first.

AMD has few symptoms in the early stages, so it is important to have your eyes examined regularly. If you are at risk for AMD because of age, family history, lifestyle, or some combination of these factors, you should not wait to experience changes in vision before getting checked for AMD.

Not everyone with early AMD will develop late AMD. For people who have early AMD in one eye and no signs of AMD in the other eye, about five percent will develop advanced AMD after 10 years. For people who have early AMD in both eyes, about 14 percent will develop late AMD in at least one eye after 10 years. With prompt detection of AMD, there are steps you can take to further reduce your risk of vision loss from late AMD.

If you have late AMD in one eye only, you may not notice any changes in your overall vision. With the other eye seeing clearly, you may still be able to drive, read, and see fine details. However, having late AMD in one eye means you are at increased risk for late AMD in your other eye. If you notice distortion or blurred vision, even if it doesnt have much effect on your daily life, consult an eye care professional.

Questions to ask your eye care professional about treatment

- What is the treatment for advanced neovascular AMD?
- When will treatment start and how long will it last?
- What are the benefits of this treatment and how successful is it?
- What are the risks and side effects associated with this treatment and how has this information been gathered?
- Should I avoid certain foods, drugs, or activities while I am undergoing treatment?
- Are other treatments available?
- When should I follow up after treatment?

Loss of Vision

Coping with AMD and vision loss can be a traumatic experience. This is especially true if you have just begun to lose your vision or have low vision. Having low vision means that even with regular glasses, contact lenses, medicine, or surgery, you find everyday tasks difficult to do. Reading the mail, shopping, cooking, and writing can all seem challenging.

However, help is available. You may not be able to restore your vision, but low vision services can help you make the most of what is remaining. You can continue enjoying friends, family, hobbies, and other interests just as you always have. The key is to not delay use of these services.

What is vision rehabilitation?

To cope with vision loss, you must first have an excellent support team. This team should include you, your primary eye care professional, and an optometrist or ophthalmologist specializing in low vision. Occupational therapists, orientation and mobility specialists, certified low vision therapists, counselors, and social workers are also available to help. Together, the low vision team can help you make the most of your remaining vision and maintain your independence.

Second, talk with your eye care professional about your vision problems. Ask about vision rehabilitation, even if your eye care professional says that "nothing more can be done for your vision." Vision rehabilitation programs offer a wide range of services, including training for magnifying and adaptive devices, ways to complete daily living skills safely and independently, guidance on modifying your home, and information on where to locate resources and support to help you cope with your vision loss.

Where to go for services

Low vision services can take place in different locations, including:

- Ophthalmology or optometry offices that specialize in low vision
- Hospital clinics
- State, nonprofit, or for-profit vision rehabilitation organizations
- Independent-living centers

What are some low vision devices?

Because low vision varies from person to person, specialists have different tools to help patients deal with vision loss. They include:

- Reading glasses with high-powered lenses
- Handheld magnifiers
- Video magnifiers
- Computers with large-print and speech-output systems
- Large-print reading materials
- Talking watches, clocks, and calculators
- Computer aids and other technologies, such as a closed-circuit television, which uses a camera and television to enlarge printed text

For some patients with end-stage AMD, an Implantable Miniature Telescope (IMT) may be an option. This FDA-approved device can help restore some lost vision by refocusing images onto a healthier part of the retina. After the surgery to implant the IMT, patients participate in an extensive vision rehabilitation program.

Keep in mind that low vision aids without proper diagnosis, evaluation, and training may not work for you. It is important that you work closely with your low vision team to get the best device or combination of aids to help improve your ability to see.

Questions to ask your eye care professional about low vision

- How can I continue my normal, routine activities?
- Are there resources to help me?
- Will any special devices help me with reading, cooking, or fixing things around the house?
- What training is available to me?
- Where can I find individual or group support to cope with my vision loss?

Coping with AMD

AMD and vision loss can profoundly affect your life. This is especially true if you lose your vision rapidly.

Even if you experience gradual vision loss, you may not be able to live your life the way you used to. You may need to cut back on working, volunteering, and recreational activities. Your relationships may change, and you may need more help from family and friends than you are used to. These changes can lead to feelings of loss, lowered self-esteem, isolation, and depression.

In addition to getting medical treatment for AMD, there are things you can do to cope:

- Learn more about your vision loss.
- Visit a specialist in low vision and get devices and learning skills to help you with the tasks of everyday living.
- Try to stay positive. People who remain hopeful say they are better able to cope with AMD and vision loss.
- Stay engaged with family and friends.
- Seek a professional counselor or support group. Your doctor or eye care professional may be able to refer you to one.

Information for family members

Shock, disbelief, depression, and anger are common reactions among people who are diagnosed with AMD. These feelings can subside after a few days or weeks, or they may last longer. This can be upsetting to family members and caregivers who are trying to be as caring and supportive as possible.

Following are some ideas family members might consider:

- Obtain as much information as possible about AMD and how it affects sight. Share the information with the person who has AMD.
- Find support groups and other resources within the community.
- Encourage family and friends to visit and support the person with AMD.
- Allow for grieving. This is a natural process.
- Lend support by “being there.”

What research is being done?

NEI conducts and supports research in labs and clinical centers across the country to better prevent, detect, and treat AMD.

NEI-funded research over the past decade has revealed new insight into the genetics of AMD. By screening the DNA of thousands of people with and without AMD, scientists have identified differences in genes that affect AMD risk. Armed with this knowledge, researchers are identifying key biochemical pathways involved in the disease and are exploring therapies that could interrupt these pathways. It might also be possible to develop drug therapies for AMD that are targeted specifically to a person's unique genetic risk factors.

Scientists are also exploring ways to regenerate tissues destroyed by AMD. One approach is to make stem cells from a patient's own skin or blood. In a lab, these stem cells can be specially treated to form sheets of retinal pigment epithelium (RPE)—the pigmented layer of tissue that supports the light-sensitive cells of the retina. The goal is to generate layers of RPE that can be implanted into the patient's eye to preserve vision.

The NEI Audacious Goals Initiative (AGI) is taking on one of the biggest challenges in medicine: the regeneration of nerve cells in the retina and brain. In humans, once brain and retinal neurons are gone—due to injury or diseases like AMD—they are typically gone for good. However, lessons from nature suggest that it may possible to overcome this limitation. For example, in some fish and amphibians, if the retina is damaged, it can grow back. Through targeted research, the NEI AGI aims to unlock these secrets and utilize them in humans—to develop new therapies to regenerate neurons and neural connections in the eye and visual system.

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	Chromosome is a thread-like structure of DNA that carries hereditary information, or genes. Human cells have 22 chromosome pairs plus two sex chromosomes, giving a total of 46 per cell.
GENOME	A genome is an organism's complete set of DNA, including all of its genes. Each genome contains all of the information needed to build and maintain that organism. In 2018 humans, a copy of the entire genome—more than 3 billion DNA base pairs—is contained in all cells that have a nucleus.
GENOTYPE	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 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 than 1 means that the the people with the variant are less likely to develop the condition.
PHENOTYPE	A description of an individual's physical characteristics, including appearance, development and behaviour. 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.