

Genetic Testing

When an individual is diagnosed with celiac disease, the entire family learns that they must be tested on a regular basis for the condition, for they are now at risk. First degree relatives (parent, child, sibling) have a 1 in 22 chance of developing celiac disease in their lifetimes; in second degree relatives, (aunt, uncle, cousin, grandparent) the risk is 1 in 39. Only lifetime screening can help family members reduce the long term impact of celiac disease and facilitate a quick diagnosis. They learn that regular antibody testing is necessary because celiac disease is a genetic condition and could appear again in the family at any time.

What is genetic testing and who can benefit from it?

There is a blood test available to determine whether or not an at-risk individual carries the genes responsible for the development of celiac disease. These genes are located on the HLA-class II complex and are called DQ2 and DQ8. Each case of celiac disease has been found to show these so-called "haplotypes"; therefore, a negative gene test indicates that celiac disease cannot develop in that individual.

There are two main reasons for using the genetic test when evaluating an individual for celiac disease. The first case is to "rule out" celiac disease, which is a medical term that indicates an individual does not possess a necessary risk factor for the development of celiac disease, genetic predisposition. Without this factor, it is impossible that the individual with

a negative gene test will develop celiac disease in the future. People who test negative for the gene would not be required to have regular antibody screening for the remainder of their lives. For example, the children of an adult with celiac disease could have the gene test. The results would allow the parent to know which children need close monitoring.

In individuals with symptoms who have not had a biopsy to diagnose celiac disease, but have been on the gluten-free diet for a significant period of time, the gene test is often the only way to determine if symptoms could possibly be related to celiac disease. For a person who faces this situation, a negative gene test would indicate that symptoms are not the a result of celiac disease. A positive gene test, however, does not diagnose the disease but increases the likelihood that it is present.

If I have a gene for celiac disease, does that mean I have celiac disease?

The gene test does not diagnose celiac disease. It places an individual into an “at-risk” group for celiac disease, which indicates the individual should be closely monitored with antibody testing in the future. When the genetic predisposition for celiac disease was detected (on Chromosome 6) researchers noted that the genes were a necessary but not sufficient condition for the disease to develop. In fact, up to one third of the U.S. population has the genes for celiac disease, but it is thought that only 1-4% of them will actually develop the disease at some point in their lifetimes. This means that people with DQ2 or DQ8 can develop celiac disease, but the vast majority of them aren't destined to develop it.

How is genetic testing different than antibody testing for celiac disease? The blood tests that most people with celiac disease are familiar with are the antibody tests. These tests, such as the tissue transglutaminase test (tTG) or the antiendomysial (EMA) antibody test, measure the autoimmune response triggered by gluten that occurs at a point in time. (Think of it as a photograph.) These are important tests because they characterize the extent to which the immune system is responding to gluten.

Unlike antibody testing, the HLA gene testing for celiac disease measures the presence or absence of genetically-programmed molecules that are found on the surface of some cells. The HLA gene test for celiac disease can be performed at any time after birth (and even in the cord blood at birth!)—an individual is either born with or without these factors and they do not change over time.

How is the genetic predisposition for celiac disease inherited?

Inheriting the genes for celiac disease occurs differently than the manner in which many genetic traits are passed on. We are accustomed to thinking in terms of dominant or recessive genes which are inherited from both parents and form sets to determine hair color, height, and other

human health characteristics. In fact, even though DQ2 and DQ8 are passed on similarly, they are not sufficient to determine the occurrence of the disease, even if they are present in double doses.

Because 35% of the American population have either DQ2 (more commonly) or DQ8, it is possible for two affected people to marry each other. The genes can be passed on by males as well as females. Therefore, one person's gene test doesn't necessarily mean that the other side of the family is not affected as well.

Who can order the gene test? Does it have to go to a special laboratory? How much does it cost?

Genetic testing can be expensive and can vary by geography and the type of medical center where you have it done. Costs include the cost of the actual test, the hospital laboratory fees, equipment/supplies, and processing. The test is usually ordered by a gastroenterologist. Ask your doctor's office about the cost of the test before you have it done. In addition, you should take steps to insure that your insurance company will cover the test before the blood is drawn. The test must go to a skilled laboratory for analysis, such as Prometheus Laboratories or the Mayo Clinic.

Do I have to be eating gluten for the genetic test to be reliable?

No, the presence or absence of genetic factors is not influenced by diet.

For more information contact the University of Chicago Celiac Disease Center at 773.702.7593 or www.CeliacDisease.net.