GlutenID Celiac Genetic Health Risk (GHR) Test

Package Insert/Instructions for Use

IVD

Manufactured by:

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For *in-vitro* diagnostic use

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Summary

The GlutenID Celiac Genetic Health Risk (GHR) Test is a direct-to-consumer (DTC) DNA genetic testing service for over-the-counter (OTC) use. The test creates a report that identifies the presence or absence of four HLA-DQ haplotype variants associated with the risk of developing Celiac disease. The GlutenID Celiac GHR Test is indicated for reporting of one variant associated with the HLA-DQ2.5 haplotype, one variant associated with the HLA-DQ8 haplotype, one variant associated with the HLA-DQ7 haplotype, and three variants associated with the HLA-DQ2.2 haplotype.

The tests are conducted with genomic DNA isolated from human saliva samples collected in the FDA cleared ORAcollect®.Dx (OCD-100) device manufactured by DNA Genotek Inc. https://dnagenotek.com/globaldocs/sds/00021/PD-MSDS-00021.pdf
The GlutenID GHR Test website (https://targeted-genomics.com) provides the contents and the procedure to order and use the test service. The consumers order the test, receive a package containing the sample collection materials, and collect their sample at home. After registering the sample collection in a HIPAA compliant website portal, they mail their sample to a third-party laboratory in the pre-paid shipping box. When their result is ready, they use a secure portal to receive their test report.

The results of the testing are provided in customized reports for each user. These reports inform the user of the variant(s) detected in their sample as well as the risk of disease associated with the variants. Risk is assigned to three categories: Increased, Low, Not Likely at Risk. If no variants were detected, this information is also provided. The reports are designed to present scientific concepts to users in an easy-to- understand format. Reports provide scientific information about the possible risks associated with each variant.

GlutenID Risk Gradient for 15 GlutenID Markers

GlutenID Marker	Estimated Risk	Risk Category
DQ2+DQ2	1 in 9 (11%)	Increased
DQ2+half-DQ-DQ2	1 in 9 (11%)	
DQ2+DQ8	1 in 12 (8%)	
DQ8+half-DQ2	1 in 25 (4%)	
DQ2+DQ7	1 in 35 (3%)	
DQ2.2+DQ7 [DQ2 trans]	1 in 35 (3%)	
DQ2 (cis)	1 in 35 (3%)	
DQ8+DQ8	1 in 100 (1%)	Low
DQ8	1 in 100 (1%)	
DQ8+DQ7	1 in 100 (1%)	
half-DQ2+half-DQ2 (DQ2.2+DQ2.2)	1 in 210 (0.5%)	Not Likely at Risk
half-DQ2 (DQ2.2)	1 in 210 (0.5%)	

DQ7+DQ7	1 in 1842 (0.05%)	
DQ7	1 in 1842 (0.05%)	
Non-celiac genetics (NCG)	1 in 2518 (0.05%)	

The DQ2.5 haplotype is commonly referred to as DQ2(*cis*) while the DQ7+DQ2.2 haplotype is called DQ2(*trans*).

Intended Use/Indications for Use

The GlutenID Celiac Genetic Health Risk Test uses qualitative genotyping to detect clinically relevant variants in genomic DNA isolated from saliva collected from individuals 18 years of age or older with ORAcollect Dx OCD-100 for the purpose of reporting and interpreting Genetic Health Risks (GHR).

The GlutenID Celiac GHR Test is indicated for reporting of one variant associated with the HLA-DQ2.5 haplotype, one variant associated with the HLA-DQ8 haplotype, one variant associated with the HLA-DQ7 haplotype, and three variants associated with the HLA-DQ2.2 haplotype. The report describes if a person has variants linked to haplotypes associated with an increased risk for developing celiac disease, but it does not describe a person's overall risk of developing celiac disease. This report is most relevant for people of European descent.

Sample Collection

Materials included in the sample collection package

Component	Description	Count
ORAcollect®.Dx (OCD-100)	to collect, stabilize and protect DNA saliva samples	1

Booklet IFU	Instructions for sample collection and registration	1
USPS mailing label	Label for returning Saliva samples to the laboratory	1

Important notes to the user:

- Following saliva sample collection, swab samples are returned to the laboratory in the same tubes and box using a pre-paid mailing label affixed to the box.

- The lab will only accept samples delivered via postal service or carrier. Do not attempt to drop off your sample directly at the lab.

- The company will provide you with free replacement shipping materials if you have misplaced or discarded your return shipping supplies. If you have discarded your return shipping supplies, please contact Customer Care. The only mailed samples accepted are those returned with the pre-paid shipping materials provided by Targeted Genomics.

- In less than 1% of cases, test failure occurs due to low DNA quantity/quality. In this case the laboratory may not be able to process your sample. Targeted Genomics will send a new collection kit free of charge.

Important Warnings, Precautions, and Limitations

Relevant races/ethnicities

The variants included in this test are common in many ethnicities including White, African American, Asian, and Others but are best studied in people of European descent. The relevance of each report and how your genetic health risk results are interpreted may differ depending on your ethnicity. Each genetic health report indicates if a person has variants associated with an increased risk of developing a disease, but it does not indicate their overall risk.

WARNING:

Special Conditions for Use

- For over-the-counter (OTC) use.
- The test is intended for users ≥ 18 years old.
- This test is not a substitute for visits to a healthcare provider. It is recommended that you consult with a genetic counselor or your healthcare provider if you have any questions or concerns about your results.
- The test does not detect all genetic variants related to celiac disease. The absence of a variant tested does not rule out the presence of other genetic variants that may be disease related.
- The test does not diagnose any specific health conditions, determine medical treatment or other medical intervention, or tell the user anything about their current state of health. Only a healthcare professional can diagnose a disease or condition. Results should not be used to make medical decisions.
- The laboratory may not be able to process a patient's sample due to low DNA quantity/quality. This is estimated to occur with a frequency of less than 1%. If this happens, the user will receive an email notification.
- A user's race, ethnicity, age, sex, and lifestyle may affect how the genetic results are interpreted.

Other Warnings and Limitations:

- The minimum age threshold to self-collect a sample is >= 18 years of age
- The celiac GHR must be reported and interpreted by users 18 years of age or older.
- This test provides genetic risk information based on the specific genetic risk variants tested. It does not report on a user's entire genetic profile.
- Having a risk variant does not guarantee that you will develop a health condition. Furthermore, it is still possible that you may develop the condition without a variant being identified. These reports may not contain all genetic risk variants.
- To interpret genetic test results and use them effectively, speak with a genetic counselor or healthcare professional. Don't base your medical decisions on genetic results.

- Variant(s) not detected: You do not have the variant(s) we tested. Since this test does not include all variants that may impact your risk of developing celiac disease, you may still have another variant that could affect your risk. Non-genetic factors may also affect your risk.

- Variant(s) detected: It is possible that you have one or more of the variants we tested. Your risk of developing celiac disease may be higher. However, this does not mean you will develop celiac disease. There are other factors that may also influence your risk.

- Neither the report nor the test is intended to tell you anything about the likelihood that you will develop a celiac disease in the future. GlutenID reports only include information related to your genetic health risk.

- The GlutenID test does not detect all genetic variants related to celiac disease. The absence of a variant tested does not rule out the presence of other variants.
- Different companies offering genetic testing for celiac disease may be analyzing different variants so you may get different results from a different test.

- Some people may feel anxious about receiving genetic health results. If you feel very anxious, you should speak to a genetic counselor or your doctor prior to collecting your sample for testing.

- If you have other risk factors for the celiac disease, you should discuss with a doctor.

- You can also discuss your results with a genetics counselor https://findageneticcounselor.nsgc.org/?reload=timezone

- Genetic Health Risk reports are intended to provide you with genetic information to inform conversations with a healthcare professional. These reports should not be used to make medical decisions. Always consult with a healthcare professional before taking any medical action.

Precautions:

Do not eat, drink, smoke, chew gum, brush your teeth, or use mouthwash for at least 30 minutes prior to providing your sample.

Do Not Reuse this Product: Risks of re-use include microbial exposures and swab breakage. Providing the DNA Sample ORAcollect®.Dx (OCD-100) instructions included with your kit about providing your Saliva sample.

(live link) https://dnagenotek.com/US/pdf/PD-MSDS-00021.pdf

WARNING: Do NOT ingest DNA stabilizing liquid in the swab tube.

Analytical Performance

Samples for the GlutenID test were collected using ORAcollect Dx OCD-100 and sequenced on the Illumina MiSeqDx. Results were analyzed using GlutenID Analysis Software supported by the Galaxy Platform. Variant calls from the technical data were translated into a final GlutenID genotype for each sample.

Accuracy

Targeted Genomics performed a method comparison study to assess accuracy of the GlutenID Celiac GHR Test. Results of the GlutenID test were compared with bi-directional Sanger sequencing results for 20 unique samples representing wild-type genotypes and 40 unique samples positive for the four celiac risk haplotypes collectively representing 150 total variants:

- HLA-DQ2.5 wildtype (CC), heterozygous (CT), homozygous (TT)
- HLA-DQ8 wildtype (TT), heterozygous (TC), homozygous (CC)
- HLA-DQ7 wildtype (GG), heterozygous (GA), homozygous (AA)
- HLA-DQ2.2 wildtype (TT), heterozygous (TC), homozygous (CC)

Agreement between the two methods and technical positive predictive value (TPPV) was 100% for all samples analyzed.

Precision/Reproducibility

Precision studies were performed to determine the consistency between independently measured test results for the GlutenID Celiac GHR Test under the following changed conditions: assay run, critical reagent lot, instrument, operator, and day. All test results yielded 100% correct calls.

Minimum DNA Input

DNA input was studied at 1 ng/uL, 5 ng/uL, and 10 ng/uL to determine the lowest concentration of DNA needed for at least 95% concordant test results. The study yielded concordant test results and passed acceptance criteria for samples at all three concentrations. Minimum input DNA concentration was set at a minimum of 1 ng/µL.

Interferences with other Substances

Studies were performed to assess whether foreign substances that may be present in the mouth affect the results of GlutenID testing. 90 swab samples self-collected by four individuals with known DQ2,DQ8, DQ2.2, DQ7 status were sent to a CLIA certified laboratory for re-testing. The samples were collected following exposure to common endogenous, exogenous, and microbial interfering substances. Interfering substances did not affect test performance.

The following interferents were tested:

- Amylase
- IgA
- Hemoglobin
- Total protein
- Eating (beef, not-beef)
- Drinking
- Chewing gum
- Smoking
- Mouthwash
- Microbial

Gluten ID Celiac GHR Test sample collection package contains ORAcollect swabs and includes instructions for Use (IFU) recommending the user NOT eat, drink, smoke, or chew gum 30 minutes before sample collection. For more information refer to the Material Safety Data sheet at Oracollect.com. https://dnagenotek.com/US/pdf/PD-MSDS-00021.pdf.

Clinical Performance

The clinical performance and variants included for the GlutenID Celiac Genetic Health Risk Test are supported by peer-reviewed scientific literature. The HLA-DQ2.5 haplotype is present in 95% of patients diagnosed with celiac disease and the HLA- DQ8 haplotype is detected in < 5%. (Taylor 2015) Rarely HLA-DQ2 is inherited in the form of two separate haplotypes HLA-DQ7 and HLA-DQ2.2 (one half from each parent) encoding alpha and beta chains differing by only two amino acids from DQ2.5 and conferring similar celiac disease risk. (Pisapia 2020)

User Studies

User comprehension studies were performed to assess how well people understand the Celiac Genetic Health Risk Test Reports. A diverse group of over 300 people answered questions about the test via an online survey. Comprehension was tested through a two-step process. First, participants' understanding of celiac genetics was tested prior to viewing the educational module. Second, participants were shown the educational module with examples from the GlutenID test reports. Participants then completed the test report comprehension survey.

Overall comprehension rates per test report concept were greater than 90% across all concepts.

FAQs and Definitions

The frequently asked questions (FAQ) section for the genetic health report can be accessed via the Test Info page of the company website: https://targeted-genomics.com/test-info/ The FAQs addresses the purpose, limitations and meaning of the results of the test. The questions included in the FAQ section for each of the tests in this submission include, but are not limited to:

- What is celiac disease?
- Can celiac disease affect anyone?
- How is celiac disease treated?
- What is the purpose of the GlutenID Test?
- Does the GlutenID test look at my whole genetic profile?
- Based on my result, should I immediately remove gluten from my diet?
- What are the limitations of the GlutenID test?
- How does this result affect my family?

For definitions of commonly used scientific terms, visit the Targeted Genomics website https://targeted-genomics.com/test-info/. Terms explained include the following:

- Autoimmune Condition
- Celiac Disease
- Celiac Risk Variant
- DNA

- Gene
- Dietary Gluten
- Gluten Free Diet
- Gluten Sensitivity
- Haplotype
- Immune System

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