Package Insert
GlutenID Celiac Genetic Health Risk (GHR) Test

Manufactured by:

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IVD

For *in-vitro* diagnostic use

Table of Contents

1. Summary and Intended Use

Summary

The Celiac GHR test can be ordered and used at home to learn about your Celiac GHR from DNA extracted from the buccal cells inside your cheeks. The test works by detecting specific gene variants associated with Celiac Disease. Your genetic results are reported to you by Targeted Genomics via secure email.

Intended Use

The GlutenID Celiac Genetic Health Risk (GHR) Test uses qualitative genotyping to detect clinically relevant variants in genomic DNA isolated from human buccal (cheek) cells collected by individuals ≥ 18 years with the COPAN FLOQSwabs for the purpose of reporting and interpreting celiac GHR.

Indications for Use

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 GlutenID report describes if a person has variants linked to a haplotype 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.

Special considerations

- Genetic testing for celiac disease is recommended under certain circumstances by several health professional organizations, including the College of American Pathologists (CAP) and the American College of Gastroenterology. Refer to the CAP and Amercian College of Gastroenterology guidelines for the latest recommendations about when genetic testing for celiac disease is appropriate.

2. Important Limitations and Warnings

Important Considerations

- Be sure to follow the Cheek Swab Collection Kit instructions to ensure DNA results can be processed by the laboratory.
- Your ethnicity may affect whether the GlutenID Celiac GHR test is relevant for you.
- Other environmental and lifestyle factors may affect your risk of developing celiac disease.
- If you have a family history of celiac disease or are experiencing symptoms, consult with your healthcare provider about appropriate diagnostic testing.
- The GlutenID test cannot determine your overall risk for developing celiac disease in the future.
- The GlutenID test is not intended to diagnose celiac disease or any other health condition.
- GlutenID is not intended for prenatal testing.
- The laboratory may not be able to process your sample. If this occurs, you will be notified via email and offered one free replacement kit for sending a new sample.

Limitations

- The GlutenID test is intended to identify celiac genetic risk for users 18 years and above. A user may self-administer or administer the test for another person.
- 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.
- 24 potentially interfering mutations were identified for HLA-DQ2.5, HLA-DQ8, HLA-2.2, HLA-DQ7. Interference due to these mutations on the performance of the assay has not been evaluated.
- The GlutenID test is not a substitute for visits to a healthcare professional. You should consult with a healthcare professional if you have questions or concerns about your results.
- 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. This is normal. If you feel very anxious, you should speak to your doctor or a genetic counselor prior to collecting your sample for testing. You may also consider getting your celiac GHR testing done by your doctor.

Warnings

- For oral use only. Do not swallow or use the kit swabs for any other purpose. The small cap of the swab container may pose a choking hazard.
- Store and transport GlutenID kit at ambient temperature (68º -72ºF), not colder than -112ºF.

For Healthcare Professionals

- The GlutenID test is not intended to diagnose celiac disease, determine medical treatment, or tell the user anything about their current state of health.
- The GlutenID test is intended to provide users with their genetic information, which may inform health-related lifestyle decisions and conversations with their doctor or other healthcare professional.
- Healthcare professionals should base diagnostic or treatment decisions on testing and/or other information determined to be appropriate for each patient.

3. Test Performance

Overview

Samples for the GlutenID test were collected using COPAN FLOQSwabs 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.

Clinical Performance

The variants covered by the GlutenID GHR test are supported by the highest level (Level 1) of peer-reviewed scientific literature. The tested variants are common in many ethnicities. These variants are most often identified in people of European descent. Published medical literature estimate that 30% of people of European descent have at least one copy of the HLA-DQ2 haplotype and 5% have at least one copy of the HLA-DQ8 haplotype. The HLA-DQ2 and HLA-DQ8 haplotypes

are present in > 95% of patients diagnosed with celiac disease. The presence of one or more of the Celiac GHR risk alleles is necessary, but not sufficient for development of celiac disease. Ruling out the presence of HLA-DQ2 and HLA-DQ8 has negative predictive value (NPV) of >99% for ruling out celiac disease.

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 (AA), heterozygous (AG), homozygous (GG)
- HLA-DQ2.2 wildtype (TT), heterozygous (TG), homozygous (GG)

Agreement between the two methods 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. A total of 322 study replicates were analyzed across these different testing conditions. The precision study yielded repeatability and reproducibility of 100%.

Minimum DNA Input

DNA samples with concentrations in the range of 3.9 ng/ul-250ng/ul are eligible for further processing by the laboratory.

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. 48 swab samples self-collected by four individuals with known DQ2 and DQ8 status (previously established by GlutenID testing) were sent to PacificDx laboratory for re-testing. The samples were collected following exposure to common endogenous, exogenous, and

microbial interfering substances **before and after** rinsing the mouth with water as directed in the GlutenID instructions for use (IFU.) One sample collected before rinsing mouth yielded insufficient DNA. All other samples produced accurate DQ2/DQ8 results.

The following interferents were tested:

- Alcohol
- Protein
- Wheat
- Dairy
- Toothpaste
- Gum base
- Sugar
- Blood
- Bacteria (S. Thermophilus, L. Bulgaricus, L. Acidophilus, L. Casel, Bifidus)

Gluten ID Cheek Swab Collection (CSC) Kit contains COPAN FLOQSwabs and include instructions for Use (IFU) recommending the user rinse their mouth with water prior to swab collection of buccal cells thus minimizing the presence of interferents in the sample.

Mutations

Performance of the GlutenID Celiac GHR test may be affected by the presence of the following rare mutations:

Haplotype	**Tag SNP(s)**	**Potentially Interfering Mutations**
DQ2.5	rs2187668	rs769029321, rs1189841207, rs1490317600, rs1466681194, rs1379617295
DQ8	rs7454108	rs1398151255, rs1037255898, rs564828053, rs776920125
DQ7	rs4639334	rs1227184065, rs114929610, rs1296659658

DQ2.2	rs2395182 rs7775228	rs1562307508, rs1027315826, rs375347825, rs1022268175, rs1036852583, rs73405373, rs1042832287, rs4713587, rs72844311, rs112931959, rs1475416138,

User Studies

Cheek swab collection kit user study

User studies were performed to assess the ability of naive users to provide samples adequate for testing from home based on the kit instructions alone.

A total of 100 participants across a range of age and educational backgrounds collected and mailed swab samples from their home to the laboratory using the collection kit instructions. Cheek cell samples were processed according to standard laboratory procedures. DNA quantity and quality was assessed as evidence of successful collection.

All (100%) of samples in the study yielded adequate DNA for testing. All results were reported successfully to the users demonstrating that users from diverse backgrounds can understand the collection kit instructions and provide adequate cheek swab samples.

Celiac GHR test report user comprehension study

User comprehension studies were performed to assess how well people understand the Celiac Genetic Health Risk Test Reports. A diverse group of 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 form 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.

4. Selected References

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Singh P et al. (2018). “Global prevalence of celiac disease: systematic review and meta-analysis.” Clin Gastroenterol and Hepatol. 16:823-836. pubmed.ncbi.nlm.nih.gov/29551598/

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Taylor AK et al. (2008). "Celiac disease." [Updated 2015 Sep 17. ncbi.nlm.nih.gov/pubmed/20301720

Additional references can be found in the GlutenID Celiac GHR Test Report.

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