MAYO CLINIC LABORATORIES

Test Definition: CELI

Celiac Associated HLA-DQ Alpha 1 and DQ Beta 1 DNA Typing, Blood

Overview

Useful For

Assessing risk of celiac disease

Testing Algorithm

The following algorithms are available:

-Celiac Disease Comprehensive Cascade Test Algorithm

-Celiac Disease Diagnostic Testing Algorithm

-Celiac Disease Gluten-Free Cascade Test Algorithm

-Celiac Disease Routine Treatment Monitoring Algorithm

-Celiac Disease Serology Cascade Test Algorithm

Special Instructions

- Celiac Disease Diagnostic Testing Algorithm
- Celiac Disease Comprehensive Cascade Test Algorithm
- Celiac Disease Gluten-Free Cascade Test Algorithm
- Celiac Disease Routine Treatment Monitoring Algorithm
- Celiac Disease Serology Cascade Test Algorithm

Method Name

Polymerase Chain Reaction (PCR)/Sequence-Specific Oligonucleotide Probe (SSO)

NY State Available

Yes

Specimen

Specimen Type

Whole Blood ACD-B

Ordering Guidance

Cascade testing is recommended for celiac disease. Cascade testing ensures that testing proceeds in an algorithmic fashion. The following cascades are available; select the appropriate one for your specific patient situation.

-CDCOM / Celiac Disease Comprehensive Cascade, Serum and Whole Blood: complete testing including HLA DQ

-CDSP / Celiac Disease Serology Cascade, Serum: complete testing excluding HLA DQ

-CDGF / Celiac Disease Gluten-Free Cascade, Serum and Whole Blood: for patients already adhering to a gluten-free diet

To order individual tests, see Celiac Disease Diagnostic Testing Algorithm.

Specimen Required

Container/Tube: Yellow top (ACD Solution A or B)
Specimen Volume: 6 mL
Collection Instructions: Send whole blood specimen in original tube. **Do not aliquot.**

Forms

If not ordering electronically, complete, print, and send Gastroenterology and Hepatology Test Request (T728) with the specimen.

Specimen Minimum Volume

3 mL

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole Blood ACD-B	Ambient		
	Refrigerated (preferred)		

Clinical & Interpretive

Clinical Information

Celiac disease (gluten-sensitive enteropathy) is mediated by T lymphocytes in patients with genetic susceptibility. This genetic association is with certain HLA genes in the class II region (DQ alpha 1, DQ beta 1).

Reference Values

An interpretive report will be provided.

Interpretation

Most (90%-95%) patients with celiac disease have 1 or 2 copies of HLA-DQ2 haplotype (see below), while the remainder have HLA-DQ8 haplotype. Rare exceptions to these associations have been occasionally seen. In one study of celiac disease, only 0.7% of patients with celiac disease lacked the HLA alleles mentioned above. Results are reported as permissive, nonpermissive, or equivocal gene pairs.

It is important to realize that these genes are also present in about 20% of people without celiac disease. Therefore, the mere presence of these genes does not prove the presence of celiac disease or that genetic susceptibility to celiac disease is present.

The HLA-DQ molecule is composed of 2 chains: DQ alpha (encoded by *HLA-DQA1* gene) and DQ beta (encoded by *HLA-DQB1* gene). HLA-DQ typing can be performed by serological or molecular methods. Currently, most laboratories perform typing by molecular methods. HLA-DQ2 and DQ8, as typed by serology, are usually based on the molecular typing of the DQB1 chain only. The current molecular method allows typing for both the DQB1 and DQA1 chains. This

has shown that there are different haplotypes of HLA-DQ2 and DQ8. Typing of these haplotypes is important in celiac disease as they carry different risk association.

There are 2 common haplotypes of DQ2:
1. *DQA1*05:01* with *DQB1*02:01*, also called DQ2.5 in celiac literature
2. *DQA1*02:01* with *DQB1*02:02*, also called DQ2.2 in celiac literature
A single haplotype (heterozygote) of DQ2.5 is permissive for presence of celiac genes. However, only a double haplotype (homozygous) of DQ2.2 is permissive for presence of celiac genes. There are few reports where a single haplotype of DQ2.2 is considered to be an equivocal risk. In some cases, the DQ2.2 haplotype may be present with a DQ7.5 haplotype (*DQA1*05:05* with *DQB1*03:01*). In this case, a DQ2.5 molecule can be formed by the combination of *DQB1*02:02* from one chromosome and *DQA1*05:05* from the other chromosome. These cases fall in the same category as the DQ2.5 heterozygote.

There are 3 common haplotypes of DQ8:
1. *DQA1*03:01* with *DQB1*03:02*
2. *DQA1*03:02* with *DQB1*03:02*
3. *DQA1*03:03* with *DQB1*03:02*
Any single haplotype (heterozygote) of DQ8 is permissive for celiac.

Therefore, the gene pairs permissive for celiac are:
1. Heterozygote (single copy)
-*DQA1*05:XX* with *DQB1*02:01*
-*DQA1*05:XX* with *DQB1*02:02*
-*DQA1*03:XX* with *DQB1*03:02*
2. Homozygous (2 copies)
-*DQA1*02:01* with *DQB1*02:02*

Gene pairs equivocal for celiac are:
1. Heterozygote (single copy)
-*DQA1*02:01* with *DQB1*02:02*
2. Rare allele's types of DQ2 and DQ8 other than those listed above

All other gene pair combinations are considered nonpermissive for celiac.

There are reports that specific HLA-DQ2 and DQ8 combinations may confer different risks for the development of celiac disease.(1)

A recent publication from our group demonstrated that risk gradient of tissue transglutaminase (tTG) IgA positivity depends on specific HLA-DQ2 and DQ8 combinations.(2) For more information see Tissue Transglutaminase IgA positivity.

Cautions

Based on the catalog of common, intermediate, and well-documented alleles in the world population,(3), certain intermediate or common alleles in some ethnicities may not be resolved.

Supportive Data

This figure shows the risk gradient of tissue transglutaminase (tTG) IgA positivity according to the HLA-DQ haplotype combination. Compared with patients who had non-permissive HLA-DQ heterodimers, patients who had HLA-DQ2 homozygosity (HLA-DQ2.5/DQ2.5, HLA-DQ2.5/DQ2.2, or HLA-DQ2.2/DQ2.2) showed increased odds for tTG-IgA positivity (OR =96.9; 95% CI, 58.3–147.9, p < .0001). Patients with 1 copy of HLA-DQ2.5 also had increased odds for tTG-IgA positivity, and, interestingly, the odds for patients who were compound heterozygous for HLA-DQ2.5 and HLA-DQ8 (OR =42.3; 95% CI, 25.2–71.0, p < .0001) were similar to those for HLA-DQ2.5 heterozygotes (OR =36.8; 95% CI, 23.3–57.9, p < .0001), suggesting that a single HLA-DQ8 haplotype may not provide additional risk for tTG-IgA positivity. HLA-DQ8 carriers also showed increased odds for tTG-IgA positivity.(2)

Clinical Reference

1. Pietzak MM, Schofield TC, McGinniss MJ, Nakamura RM: Stratifying risk for celiac disease in a large at-risk United States population by using HLA alleles. Clin Gastroenterol Hepatol. 2009;7(9):966-971. doi:10.1016/j.cgh.2009.05.028
2. Choung RS, Mills JR, Snyder MR, Murray JA, Gandhi MJ: Celiac disease risk stratification based on HLA-DQ heterodimer (HLA-DQA1 approximately DQB1) typing in a large cohort of adults with suspected celiac disease. Hum Immunol. 2020;81(2-3):59-64. doi:10.1016/j.humimm.2020.01.006
3. Hurley CK, Kempenich J, Wadsworth K, et al: Common, intermediate and well-documented HLA alleles in world populations: CIWD version 3.0.0. HLA. 2020;95(6):516-531. doi:10.1111/tan.13811
4. Polvi A, Arranz E, Fernandez-Arequero M, et al: HLA-DQ2-negative celiac disease in Finland and Spain. Hum Immunol. 1998;59(3):169-175
5. Husby S, Murray JA, Katzka DA: AGA Clinical Practice Update on Diagnosis and Monitoring of Celiac Disease-Changing Utility of Serology and Histologic Measures: Expert Review. Gastroenterology. 2019;156(4):885-889. doi:10.1053/j.gastro.2018.12.010
6. Raiteri A, Granito A, Giamperoli A, Catenaro T, Negrini G, Tovoli F: Current guidelines for the management of celiac disease: A systematic review with comparative analysis. World J Gastroenterol. 2022;28(1):154-175. doi:10.3748/wjg.v28.i1.154

Performance

Method Description

LABType applies Luminex technology to the reverse sequence-specific oligonucleotide (SSO) DNA typing method. First, target DNA is polymerase chain reaction (PCR)-amplified using a group-specific primer. The PCR product is biotinylated, which allows it to be detected using R-phycoerythrin-conjugated streptavidin. The PCR product is denatured and allowed to rehybridize to complementary DNA probes conjugated to fluorescently coded microspheres. A flow analyzer identifies the fluorescent intensity of phycoerythrin on each microsphere. The HLA Class II allele or allele groups of the sample is determined by the positive and negative bead ID's using a computer software program. The assignment of the HLA typing is based on the reaction pattern compared to patterns associated with published HLA gene sequences.(Package insert: LABType SSO Typing. One Lambda; Version 04, 11/11/2019)

PDF Report

No

Day(s) Performed
Monday through Friday

Report Available
3 to 8 days

Specimen Retention Time
14 days

Performing Laboratory Location
Rochester

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test has been modified from the manufacturer's instructions. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
81376 x 2-HLA Class II typing, low resolution (eg, antigen equivalents); one locus (eg, HLA-DRB1/3/4/5, -DQB1, -DQA1, -DPB1, or -DPA1), each

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CELI	Celiac Associated HLA-DQ Typing	94492-6

Result ID	Test Result Name	Result LOINC® Value
DQA	DQ alpha 1	94495-9
DQB	DQ beta 1	53938-7
CELIG	Celiac gene pairs present?	48767-8
CELIC	Interpretation	69048-7