# Celiac Disease HLA-DQ Genotyping

Celiac disease (CD) is a chronic autoimmune-mediated disorder characterized by small intestinal damage related to gluten consumption. Manifestations of CD vary greatly between affected individuals but may include symptoms such as malabsorption, weight loss, vomiting, chronic fatigue, iron deficiency anemia, depression, headaches, and peripheral neuropathy.

For additional information, refer to Celiac Disease on ARUP Consult.

## Tests to Consider

Celiac Disease HLA-DQ Genotyping 3004445

**Method:** Polymerase Chain Reaction/Massively Parallel Sequencing, or Polymerase Chain Reaction/Sequence-Specific Oligonucleotide Probe Hybridization

- May be useful to rule out CD in selective clinical situations (eg, when a patient has started a gluten-free diet prior to testing or when small bowel histologic findings are equivocal) or to identify risk (eg, in individuals who have first-degree family members with CD)
- Not recommended for use in the initial evaluation of CD

## *HLA-DQ* in Celiac Disease

Associations of *HLA-DQ2* and *HLA-DQ8* with CD are among the strongest *HLA*-disease associations currently known. *HLA-DQ2*, often composed of alleles HLA-DQA1*05 and HLA-DQB1*02 (which encode the DQ2.5 heterodimer), is present in approximately 90% of patients with CD. The remaining 5-10% of patients with CD carry *HLA-DQ8*, most frequently composed of alleles HLA-DQA1*03 and HLA-DQB1*03:02 (which encode the DQ8 heterodimer). A minority of patients negative for the above genotypes may produce the DQ2.2 heterodimer, commonly encoded by alleles HLA-DQA1*02 and HLA-DQB1*02. When combined with either DQ2.5 or DQ8, this heterodimer may further increase the risk of CD.[1]

When HLA testing is clinically indicated, the overall genetic risk of CD in individuals with CD-associated genotypes can be stratified by gene dose and allele combination. Several studies have demonstrated that *HLA-DQ2* or *HLA-DQ8* homozygosity increases the risk of CD and its severity in symptomatic patients, compared to patients with only single copies of the permissive alleles.[1,2,3] See Stratified Genetic Risk for Patients With CD-Associated Genotypes.

## Genetics

### Gene(s)

*HLA-DQA1* and *HLA-DQB1*

### Inheritance

Multifactorial

### Incidence

Approximately 1:133 individuals in the United States

## Test Interpretation

### Clinical Sensitivity

>99%

### Analytical Sensitivity/Specificity

>99%

### Results

**Stratified Genetic Risk Patients With CD-Associated Genotypes**

| Genotype | Risk of CD[a] |
|---|---|
| DQ2.5[b] homozygous | Very high (>1:10) |
| DQ2.5[b] + DQB1*02 | Very high (>1:10) |
| DQ2.5[b] + DQ8[c] | High (>1:20) |
| DQ8 homozygous | High (>1:20) |

[a]Risk is defined according to HLA allele combinations considering a disease prevalence of 1:100. However, these alleles are common in the general population and most individuals positive for celiac-associated alleles do not develop the disease.

[b]DQ2.5 heterodimer is encoded by DQB1*02 and DQA1*05 family alleles.

[c]DQ8 heterodimer is encoded by DQB1*03:02, often in combination with DQA1*03 family alleles.

Sources: Almeida, 2016[1]; Megiorni, 2008[2]; Vader, 2003[3]; Pietzak, 2009[4]

| Genotype | Risk of CD[a] |
|---|---|
| DQ8[c] + DQB1*02 (without DQA1*05) | Intermediate (>1:50) |
| DQ2.5[b] heterozygous | Intermediate (>1:50) |
| DQ8[c] heterozygous | At risk (>1:100) |
| Unknown genotype | Average (1:100) |
| DQB1*02 (without DQA1*05) | Low |
| DQA1*05 (without DQB1*02) | Minimal |
| Negative for DQ2 and DQ8 | Not at risk |

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## Limitations

- Rare diagnostic errors may occur due to primer site variants.
- Other genetic and nongenetic factors that influence CD are not evaluated.
- Detection of celiac-associated alleles supports but does not establish a diagnosis of CD.

## References


1. Almeida LM, Gandolfi L, Pratesi R, et al. Presence of DQ2.2 associated with DQ2.5 increases the risk for celiac disease. Autoimmune Dis. 2016;2016:5409653.

2. Megiorni F, Mora B, Bonamico M, et al. HLA-DQ and risk gradient for celiac disease. Hum Immunol. 2009;70(1):55-59.

3. Vader W, Stepniak D, Kooy Y, et al. The HLA-DQ2 gene dose effect in celiac disease is directly related to the magnitude and breadth of gluten-specific T cell responses. Proc Natl Acad Sci U S A. 2003;100(21):12390-12395.

4. Pietzak MM, Schofield TC, McGinniss MJ, et al. 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.


## Related Information

Celiac Disease


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