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.

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

Because a majority of the general population carry alleles associated with celiac disease but are unaffected by it, a positive result can be used to support but not establish a diagnosis. 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.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

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Risk of CD&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>DQ2.5&lt;sup&gt;b&lt;/sup&gt; homozygous</td>
<td>Very high (&gt;1:10)</td>
</tr>
<tr>
<td>DQ2.5&lt;sup&gt;b&lt;/sup&gt; + DQB1*02</td>
<td>Very high (&gt;1:10)</td>
</tr>
<tr>
<td>DQ2.5&lt;sup&gt;b&lt;/sup&gt; + DQ8&lt;sup&gt;c&lt;/sup&gt;</td>
<td>High (&gt;1:20)</td>
</tr>
<tr>
<td>DQ8 homozygous</td>
<td>High (&gt;1:20)</td>
</tr>
<tr>
<td>DQ8&lt;sup&gt;c&lt;/sup&gt; + DQB1<em>02 (without DQA1</em>05)</td>
<td>Intermediate (&gt;1:50)</td>
</tr>
<tr>
<td>DQ2.5&lt;sup&gt;b&lt;/sup&gt; heterozygous</td>
<td>Intermediate (&gt;1:50)</td>
</tr>
<tr>
<td>DQ8&lt;sup&gt;c&lt;/sup&gt; heterozygous</td>
<td>At risk (&gt;1:100)</td>
</tr>
<tr>
<td>Unknown genotype</td>
<td>Average (1:100)</td>
</tr>
<tr>
<td>DQB1<em>02 (without DQA1</em>05)</td>
<td>Low</td>
</tr>
<tr>
<td>DQA1<em>05 (without DQB1</em>02)</td>
<td>Minimal</td>
</tr>
<tr>
<td>Negative for DQ2 and DQ8</td>
<td>Not at risk</td>
</tr>
</tbody>
</table>

<sup>a</sup>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.

<sup>b</sup>DQ2.5 heterodimer is encoded by DQB1*02 and DQA1*05 family alleles.

<sup>c</sup>DQ8 heterodimer is encoded by DQB1*03:02, often in combination with DQA1*03 family alleles.

Sources: Almeida, 2016<sup>1</sup>; Megiorni, 2008<sup>2</sup>; Vader, 2003<sup>3</sup>; Pietzak, 2009<sup>4</sup>

### 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


### Related Information
#### Celiac Disease

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