

Genetics (Gene Testing)

Key Points

- HLA-DQ2 and DQ8 are genes that are necessary but not sufficient for the development of celiac disease (CD). HLA-DQ2 (95%) and/or DQ8 (5%) is present in almost all patients with CD. ^{1,2}
 - 30-40% of the general population carries these genes, but only 3% of individuals with these genes develop CD. People without these genes are not likely to develop CD. ^{3,4}
 - HLA-DQ2 /DQ8 testing is not routinely recommended in the initial diagnosis of CD. ^{4,5}
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More on Genetic Testing

- Negative tests for both of these genes makes CD highly unlikely (negative predictive value >99%). The genetic test is valuable for analysis of subjects with an equivocal diagnosis. For example:
 - (a) Equivocal small-bowel histological finding in patients who are not producing celiac antibodies
 - (b) Evaluation of patients on a gluten-free diet (GFD) in whom no testing for CD was done before GFD was started
 - (c) Patients with discrepant celiac-specific serology and histology
 - (d) Patients with refractory CD in which we want to confirm the initial diagnosis of CD
 - (e) Patients with Down's syndrome. ^{4,6}
- Genetic analysis can also be used to rule out CD, and the subsequent need for further testing in individuals at high risk because of family history. Although only one third of family members will be spared repeated testing, particular combinations (e.g., homozygosity for DQ2) increase the risk for CD (by up to 40%). ^{6,7} On the other hand, it is possible that a child can carry DQ2 or DQ8 while both parents do not; each HLA has 2 segments and one-half of HLA DQ2 or DQ8 could be transmitted by each parent.
- Other non-HLA genes and environmental factors may contribute to the development of CD. Current research is exploring what other factors contribute to the disease, and may help us come up with better treatments or prevention. ⁴
- Genes do not change during your lifetime, so they are not affected by a GFD. ⁴
- These genes are also associated with other autoimmune conditions such as type 1 diabetes and autoimmune thyroid disease. ⁶

- Of note, gastrointestinal symptoms are improved by the GFD in the absence of CD in about 60% of patients with diarrhea predominant irritable bowel syndrome, especially those with HLA-DQ2.⁸
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Take Home Messages:

1. Most people who carry the DQ2 or DQ8 genes will never develop CD.
 2. If you do not have these genes, then you probably do not have CD.
 3. Genetic tests are not used routinely for the initial diagnosis of CD. In select clinical situations, the celiac gene test can effectively rule out CD.
 4. These genes are also present in other autoimmune conditions such as type 1 diabetes and autoimmune thyroid disease.
 5. Any tissue sample can be used for genetic testing.
 6. You do not need to be on a GFD to have the gene test.
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