

Celiac Disease (*HLA-DQA* and *HLA-DQB*) Genotyping

TO EXCLUDE A DIAGNOSIS OF CELIAC DISEASE IN A SYMPTOMATIC INDIVIDUAL OR AN AT-RISK RELATIVE OF AN AFFECTED INDIVIDUAL AND TO PROVIDE ADDITIONAL EVIDENCE FOR A DIAGNOSIS OF CELIAC DISEASE IN A SYMPTOMATIC INDIVIDUAL

Clinical Background

- Celiac disease is a systemic autoimmune disorder that is most commonly associated with gastrointestinal symptoms, including diarrhea, weight loss, anorexia, lactose intolerance, and abdominal distention and discomfort.
- The presence of non-gastrointestinal characteristics are highly variable but include: chronic fatigue, joint pain/inflammation, migraines, epilepsy, depression, attention deficit disorder, iron-deficiency anemia, vitamin deficiency, osteoporosis/osteopenia, short stature, delayed puberty, dental enamel defects, infertility, recurrent fetal loss, and dermatitis herpetiformis.
- Most commonly, affected individuals have no gastrointestinal symptoms (non-classic disease).
- Diagnosis is based on the following:
 - Classic histological findings from small bowel biopsy
 - Histologic or clinical improvement after adherence to a gluten-free diet
 - Celiac disease-associated antibodies
 - Specific allelic variants in two HLA genes: *HLA-DQA* and *HLA-DQB*
- Although celiac disease can be diagnosed at any age, the peak age for a diagnosis in adults is 30–50 years. Average time between development of symptoms and diagnosis is 11 years due to the high variability of symptoms that overlap with many other conditions.
- 30 percent of the general population has an HLA variant associated with celiac disease. Only 3 percent of individuals with such variants develop celiac disease.
- Treatment consists of adherence to a strict gluten-free diet (i.e., no wheat, rye, or barley).

Epidemiology/ Incidence

- Celiac disease has a prevalence of one in 133 in the United States.
- Common in the United States, Europe, Australia, Mexico, some South American countries, and parts of northwest India.

Genetics

- Celiac disease is only present in individuals with HLA class II antigens DQ2 and DQ8.
- The *HLA-DQ2* heterodimer is composed of the *HLA-DQA*05* and *HLA-DQB*02* alleles. DQ2 is present in more than 90 percent of affected individuals and 20–30 percent of the general population.

- The *HLA-DQ8* heterodimer is composed of the *HLA-DQA*03* and *HLA-DQB*03:02* alleles. DQ8 is present in 10 percent of the general population and 5–10 percent of individuals with celiac disease.

Indications for Ordering

- Symptomatic individuals with either borderline celiac-associated antibody results or ambiguous small bowel biopsy results.
- Currently asymptomatic individuals on a gluten-free diet who were previously symptomatic.
- Individuals remaining symptomatic despite a gluten-free diet.
- Family members of affected individuals.
- Evaluation of individuals with another condition that places them at increased risk for developing celiac disease (i.e., autoimmune disorders, Down syndrome, Turner syndrome, or selective IgA deficiency).

Contraindications

Prenatal testing.

Interpretation

- If none of the celiac disease-associated alleles (*HLA-DQA*05*, *HLA-DQB*02*, and *HLA-DQB*03:02*) is identified in a symptomatic individual, a diagnosis of celiac disease can be excluded.
- If both of the alleles associated with the *HLA-DQ2* heterodimer (*HLA-DQA*05* and *HLA-DQB*02*) are identified in a symptomatic individual, this is supportive of a diagnosis of celiac disease. Consideration should then be given to celiac disease antibody testing and small intestinal biopsy.
- If the *HLA-DQB*03:02* allele is identified in a symptomatic individual, this is supportive of a diagnosis of celiac disease. Consideration should then be given to celiac disease antibody testing and small intestinal biopsy.
- Identification of only one portion of the *HLA-DQ2* heterodimer (*HLA-DQA*05* or *HLA-DQB*02*) has rarely been observed in individuals with celiac disease. Therefore, it is only mildly supportive of a diagnosis.
- If none of the alleles associated with celiac disease (*HLA-DQA*05*, *HLA-DQB*02* or *HLA-DQB*03:02*) is identified in a relative of an individual with celiac disease, no further testing is needed as this individual is not at risk for developing celiac disease.

- If both of the alleles associated with the *HLA-DQ2* heterodimer (*HLA-DQA*05* and *HLA-DQB*02*) are identified in an asymptomatic relative of an individual with celiac disease, then celiac disease antibody testing should be conducted at three- to five-year intervals.
- If the *HLA-DQB*03:02* allele is identified in an asymptomatic relative of an individual with celiac disease, then celiac disease antibody testing should be conducted at three- to five-year intervals.

Methodology

- PCR with melting-curve analysis of the *HLA-DQA* and *HLA-DQB* loci. Analytic sensitivity and specificity are 99 percent for the *HLA-DQA*05*, *HLA-DQB*02*, and/or, *HLA-DQB*03:02* alleles.
- Clinical sensitivity is approximately 100 percent, and clinical specificity is 3 percent.

Related Tests

- *HLA-DQB* Genotyping (2002810)
- Celiac Disease Reflexive Panel (0051065)
- Celiac Disease Dual Antigen Screen (0051689)

- Deamidated Gliadin Peptide (DGP) Antibodies, IgA and IgG (0051358)
- Deamidated Gliadin Peptide (DGP) Antibody, IgA (0051357)
- Deamidated Gliadin Peptide (DGP) Antibody, IgG (0051359)
- Tissue Transglutaminase (tTG) Antibody, IgA with Reflex to Endomysial Antibody, AgA Titer by IFA (0050734)
- Tissue Transglutaminase Antibody, IgG (0056009)

References

1. Bonamico M, et al. Serologic and genetic markers of celiac disease: a sequential study in the screening of first degree relatives. *J Ped Gastro Nutr* 2006;42:150–4.
2. Green PH. The many faces of celiac disease: clinical presentation of celiac disease in the adult population. *Gastro* 2005;128:S74–8.
3. Sollid LM, Lie BA. Celiac disease genetics: current concepts and practical applications. *Clin Gastro Hepatol* 2005;3:843–51.
4. Zubillaga P, et al, HLA-DQA1 and HLA-DQB1 genetic markers and clinical presentation in celiac disease. *J Ped Gastro Nutr* 2002;34:548–54.

Test Information

2005018 Celiac Disease (*HLA-DQA1*05*, *HLA-DQB1*02*, and *HLA-DQB1*03:02*) Genotyping

For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.