HLA Typing for Celiac Disease

Versiti provides HLA typing with interpretation for celiac disease risk. Patients with certain HLA alleles in HLA-DQA1 & HLA-DQB1 genes are predisposed to celiac disease.

Celiac disease (CD) or gluten-sensitive enteropathy is an autoimmune disease and the genetic risk is assessed based on HLA-DQA1 and HLA-DQB1 molecular typing results. CD is known to be associated with HLA DQ2 and DQ8 serologic genotypes. Among CD patients, >90% carry the DQ2.5 genotype with or without the CD-associated DQ2.2 and DQ8 genotypes. Between 5-10% of CD patients carry one or two copies of DQ8 in the absence of DQ2. A very small percentage of CD patients carry other DQ alleles or one-half of the DQA1/DQB1 heterodimers described above. Genotyping risk assessment in patients with suspected CD is based on the references cited below. The presence of an at-risk genotype does not confer a diagnosis of CD and has a low positive predictive value for CD in the general population.

HLA-DQA1 & -DQB1 typing associated with the CD serotypes[1]:

HLA serotype	HLA molecular typing allele group
DQ2.2	HLA-DQB1*02 with DQA1*02
DQ2.5	HLA-DQB1*02 with DQA1*05
DQ8	HLA-DQB1*03:02 with DQA1*03

Note for DQ8: Any HLA-DQB1 alleles other than DQB1*03:02 which are associated with a DQ8 serologic equivalent and will be reported in the Extremely Low risk category.

Celiac disease genetic risk categories[2]:

Very High: DQ2.5 + DQ2.5

Very High: DQ2.5 + DQ2.2

Very High: DQ2.5 + DQ8

High: DQ2.5 + any other DQ (not DQ2.5, DQ2.2 or DQ8)

High: DQ8 + DQ8

High: DQ8 + DQ2.2

High: DQ8 + any other DQ (not DQ2.5, DQ2.2 or DQ8)

High: DQ2.2 + DQ2.2

Low: DQ2.2 + any other DQ (not DQ2.5, DQ2.2 or DQ8)

Extremely Low: any DQ combinations which do not include DQ2.5, DQ2.2 or DQ8

Indications for testing:

- Determine genetic susceptibility to celiac disease (CD)
- Rule out as a diagnosis

Test method:

Intermediate resolution HLA typing is routinely performed by PCR-rSSO. Some alleles may have been assigned based on their population frequency. Common alleles are reported in lieu of Intermediate, Well Documented or Rare alleles found at very low or unknown population frequencies.

PCR-rSSO by Luminex™ flow microfluorimetry: DNA is isolated and amplified utilizing PCR and primers specific for the DRB1 and DQB1/DQA1 loci within the HLA complex. Amplified DNA is then allowed to hybridize to sequence-specific probes that are conjugated to fluorescently-labeled microspheres. Each of these microspheres has a unique fluorescent label and collectively make up the Luminex™ liquid bead array. Hybridization events are detected fluorometrically using Luminex™ instrumentation.

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Assay sensitivity and limitations:

The test identifies associated HLA alleles that predispose the patient to developing the disorder but is not diagnostic of celiac disease. More than 95% of celiac disease patients are positive for DQ2 or DQ8, but many individuals with these genetic results do not develop celiac disease. When only a single antigen or allele is detected, it likely indicates homozygosity and is reported accordingly. However, additional testing would be required for confirmation. This test was developed and its performance characteristics determined by Versiti Wisconsin, Inc. It has not been cleared or approved by the US Food and Drug Administration. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high complexity clinical laboratory testing.

Reporting of results:

The report includes intermediate resolution of HLA-DQA1 and HLA-DQB1 genotypes and the associated serologic equivalents. Additionally, DQ2.2, DQ2.5, and DQ8 status will each be reported as positive or negative and the associated celiac disease genetic risk will be provided as Very High, High, Low, or Extremely Low.

Intermediate resolution HLA typing is reported with the use of NMDP codes. A list of all unresolved HLA alleles reported with NMDP codes can be retrieved electronically by referring to the NMDP website and utilizing the multiple allele code (MAC) designation look up tool, currently found at **https://hml.nmdp.org/MacUI/** and available via a link from **https://bioinformatics.bethematchclinical.org/hla-resources/allele-codes/**. Serologic equivalents have been assigned based on the publication "Nomenclature for factors of the HLA system, 2010" by Marsh et al. 2010, Tissue Antigens 75, 291-455, or the publication "The HLA dictionary 2008: a summary of HLA-A, -B, -C, -DRB1/3/4/5, and –DQB1 alleles and their association with serologically defined HLA-A, -B, -C, -DR, and –DQ antigen" by Holdsworth et al. 2009, Tissue Antigens 73, 95-170.

Specimen requirements:

4 buccal swabs or 14 ml EDTA (lavender top) whole blood.

SHIP

Shipping requirements:

Place the room temperature specimen and requisition into plastic bags, seal and place in an insulated container. Seal the container and place in a sturdy cardboard container and tape securely. Ship the package in compliance with your overnight carrier guidelines. Address the package to:

Client Services/Histocompatibility Laboratory
Versiti
638 N. 18th St
Milwaukee, WI, 53233

ORDER

Required forms:

Histocompatibility Lab Non-Transplant Requisition

CPT Codes/Billing/Turnaround time:

Test code: 2277

CPT codes: For recommended CPT code, visit the Versiti.org/test menu

Turnaround time: 5-7 calendar days based on time of sample receipt.

For additional information related to shipping, billing or pricing, please contact, Versiti Client Services: (414) 937-6396 or 800-245-3117, Option 1, or labinfo@versiti.org.

References:

1. Choung, R.S., J.R. Mills, M.R. Snyder, J.A. Murray and M.J. Gandhi. Celiac disease risk stratification based on HLA-DQ heterodimer (HLA-DQA1~DQB1) typing in a large cohort of adults with suspected celiac disease. Human Immunology 2020; 81: 59-64.
2. Pietzak, M.M., T.C. Schofield, M.J. McGinniss and R.M. Nakamura. Stratifying risk for celiac disease in a large at-risk United States population by using HLA alleles. Clinical Gastroenterology and Hepatology. 2009; 7:966-971.

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