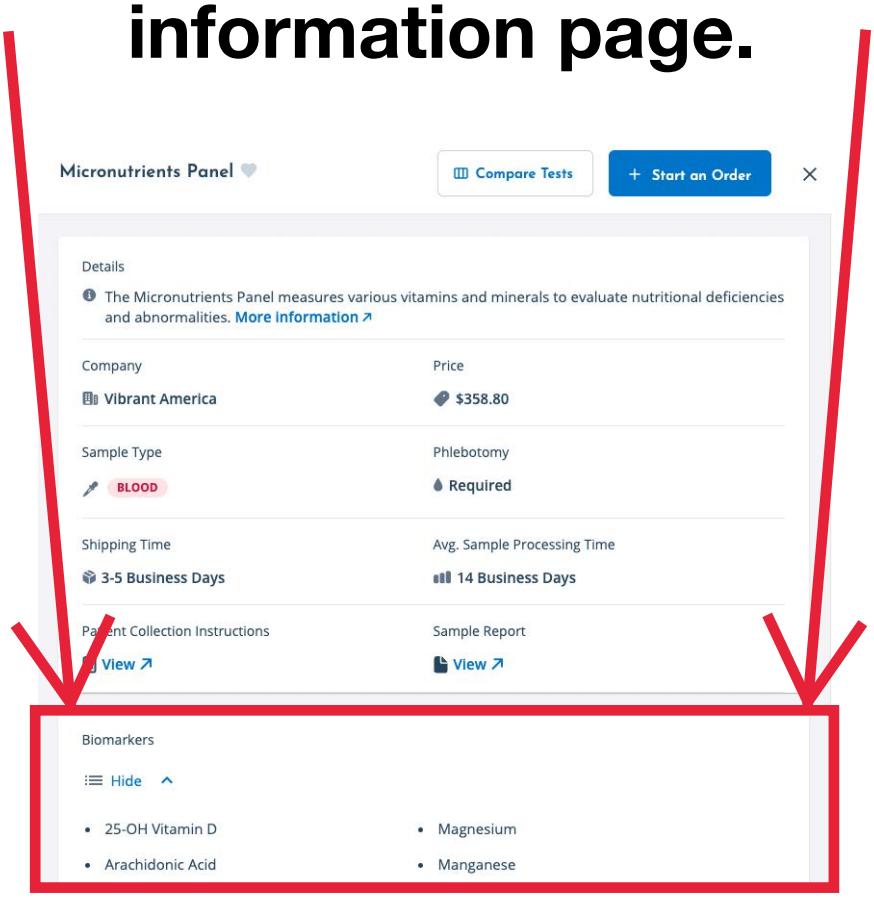
PLEASE NOTE:

Vibrant America does not provide individual test sample reports.

This report simply shows how results from Vibrant America are presented.

To determine the markers in a specific panel, please refer to the "Biomarkers" section of the Rupa Health test information page.



LAST NAME	FIRST NAME	GENDER	DATE OF BIRTH	ACCESSION ID	DATE OF SERVICE
VIBRANT AMERICA	DEMO	MALE	1996-11-29	1905130043	05-12-2019 09:43

Total IgA	Current	Reference Range	Previous
Total IgA (mg/dL)	78	61~356	**28 L (04/13/2019)**

Celiac & Gluten Sensitivity

Test name	Negative	Borderline	Positive	Negative Range	Borderline Range	Positive Range	Previous
Vibrant™ Anti-tTG IgA*			2.06	≤0.94	0.95~1.05	≥1.06	2.80 04/13/2019
Vibrant™ Anti-tTG IgG*			1.09	≤0.94	0.95~1.05	≥1.06	0.46 04/13/2019
Vibrant™ Anti-DGP IgA*	0.45			≤0.94	0.95~1.05	≥1.06	2.00 04/13/2019
Vibrant™ Anti-Gliadin IgG*			3.10	≤0.94	0.95~1.05	≥1.06	1.20 04/13/2019

Celiac HLA Genetics

HLA Type Tested	Results	Potential Risk
DQ2[1]	NEGATIVE	Patient is unlikely to develop celiac disease
DQ8[1]	NEGATIVE	

Tests flagged with * were developed by and performance characteristics were determined by Vibrant America. Indicated tests are not FDA-cleared or approved. The laboratory is regulated under CLIA and is CAP certified hence qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research. Tests flagged with [1] were performed at Vibrant Genomics. Tests flagged with [2] have analytics done at Vibrant Wellness. Laboratory Director: Mervyn Sahud, MD CLIA: 05D2078809 CLF: 00346278 Vibrant America Clinical Laboratory, 1021 Howard Avenue, Suite B, San Carlos, CA 94070. Phone: +1(866)364-0963; FAX: +1(650)508-8260; Email: support@vibrant-america.com

Interpretation of Report

CELIAC HLA GENETIC TESTING

Celiac disease is caused due to antibody production against gluten in individuals having genetic susceptibility. Serologic assays for determining anti-tTG and anti-DGP antibodies are used to select patients for biopsy which is the gold standard test for celiac disease confirmation. **The celiac disease genetic test is useful in avoiding unnecessary small intestinal biopsy, gluten free diet restrictions and continued serum antibody monitoring in individuals.**

Currently DQ2 and DQ8 are the primary genetic tests in celiac disease. DQ2 was a serological test and DQ2 antibodies were used to effectively type DQ2 bearing individuals, however, these antibodies may detect DQB1*0303 which was a major drawback in this test methodology creating the need to move to gene based testing.

The table below summarizes the components of the test.

Vibrant Celiac Genetic Panel Summary Table

HLA Type	*Vibrant Panel*	*Other Panels*	*Comment*
DQ2	✓	✓	The DQ2.5 haplotype confers the single highest genetic risk for celiac disease
DQ8	✓	✓	Major risk haplotype that is tested with DQ2

The highest risk factor for developing celiac is a close family member with the disease while DQ2 is second. Due to its link to celiac disease, DQ2 has the highest association (of any HLA type) with autoimmune disease. Close to 95% of all celiac patients have DQ2 and 30% have 2 copies of DQ2. Of the DQ2 homozygotes who eat wheat, lifelong risk is between 20 and 40% to develop celiac disease.

The relationship of DQ2 and celiac disease, however, is complex because there are multiple DQ2 isoforms. The DQ $\alpha^5\beta^2$ (**DQ2.5**) isoform is strongly associated with CD. This isoform is partially encoded by the DQB1*02 genes in HLA-DQ2 positive individuals. DQB1*0201 is genetically linked to DQA1*0501 forming the DQ2.5 haplotype that encodes both α^5 and β^2 subunits. The DQ2.5 haplotype confers the single highest genetic risk for celiac disease.

The immunodominant site for DQ2.5 is on α2-gliadin. The site is a protease resistant 33mer that has 6 overlapping DQ2.5 restricted epitopes. This creates very strong binding of T-cells for DQ2.5-33mer complexes. DQ2.5 binds gliadin, but the binding is sensitive to deamidation caused by tissue transglutaminase or tTG. In almost all cases, the highest affinity sites of gluten are derived by deamidation. The HLA DQB1*0202 and it's linked DQA1* alleles (the DQ2.2 haplotype) do not produce the α^5 subunit. Hence, the DQ2.2 heterodimer cannot effectively present α- gliadin but it can present other gliadins. The antibody profile against gluten depends on the peptide fragments presented by the different isoforms. A comprehensive map of the antibody profile against components of wheat can be obtained by testing using Vibrant Wheat Zoomer Panel.

References

	REFERENCE/ABSTRACT	RATING
Celiac Genetics	**Alienke J. Monsuur, Paul I. W. de Bakker et.al. "Effective Detection of Human Leukocyte Antigen Risk Alleles in Celiac Disease Using Tag Single Nucleotide Polymorphisms"** DNA was available from three different cohorts. The Celiac Disease (CD) cohort had a high number of individuals with HLA-DQ2 risk variants, which was useful for testing the positive predictive value (PPV). A total of six SNPs were needed to predict the DQ2.2, DQ2.5, DQ7 and DQ8 risk types for CD. Typing was done in three different cohorts comprising a total of 754 persons (1512 alleles). A combination of 3 SNPs were needed for the prediction of DQ2.2 which includes rs2395182, rs7775228 and rs4713586, with an overall sensitivity of 0.992, a specificity of 0.998 and a PPV of 0.977. The tag SNP selected for prediction of DQ2.5 (rs2187668) showed an overall sensitivity of 1.000, a specificity of 0.999 and a PPV of 0.998. The tag SNP for DQ7 (rs4639334) showed an overall sensitivity of 1.000, a specificity of 0.997 and a PPV of 0.959. The tag SNP for DQ8 (rs7454108) showed an overall sensitivity of 0.991, a specificity of 0.996 and a PPV of 0.948.	★★★★★
	De Bakker PI, McVean G, Sabeti PC, Miretti MM, Green T, et al. "A high-resolution HLA and SNP haplotype map for disease association studies in the extended human MHC" This study characterizes the linkage disequilibrium patterns between the highly polymorphic HLA genes and background variation by typing the classical HLA genes and >7,500 common SNPs and deletion-insertion polymorphisms across four population samples. The analysis provides informative tag SNPs that capture much of the common variation in the MHC region and that could be used in disease association studies.	★★★★★
	Reinton N, Helgheim A, Shegarfi H, Moghaddam A "A one-step real-time PCR assay for detection of DQA1*05, DQB1*02 and DQB1*0302 to aid diagnosis of coeliac disease" This study represents a new real-time PCR assay, using sequence-specific primers (PCR-SSP) and TaqMan probes, for detection of DQB1*05, DQB1*02 (coding for DQ2) and DQB1*0302 (coding for DQ8). PCR amplification and detection of DQ2 and DQ8 was accurately and unambiguously performed from genomic DNA isolated from cell lines and human DNA. Amplification was scored digitally, without laboratory manipulation of amplified PCR products and with a higher accuracy than PCR-SSP.	★★★
	Fasano ME, Dametto E, D'Alfonso S "HLA Genotyping: Methods for the Identification of the HLA-DQ2,-DQ8 Heterodimers Implicated in Celiac Disease (CD) Susceptibility" This review article presented the principal technical methods to genotype the HLA-DQA1* and -DQB1* alleles associated with celiac disease (CD), corresponding to the serological heterodimers HLA-DQ2 and -DQ8. The methods for HLA typing described are based on the following techniques: PCR-SSP (Polymerase Chain Reaction-Sequence Specific Primers), Reverse PCR-SSOP (PCR-Sequence Specific Oligonucleotide Probes) and Real-Time PCR (RT-PCR).	★★★★
	Rostom A, Murray JA, Kagnoff MF. "American Gastroenterological Association (AGA) Institute technical review on the diagnosis and management of celiac disease" This clinical guideline addresses the diagnosis, treatment, and overall management of patients with celiac disease (CD), including an approach to the evaluation of non-responsive CD. While it is primarily directed at the care of adult patients, variations pertinent to the pediatric population have been included.	★★★★★
	Sollid LM. "Coeliac disease: Dissecting a complex inflammatory disorder" Coeliac disease is a typical complex inflammatory disorder, but this disease is unusual in that crucial genetic and environmental factors have been identified. This knowledge has allowed functional studies of the predisposing HLA molecules, the identification of antigenic epitopes and detailed studies of disease-relevant T cells in coeliac disease. This dissection of the pathogenic mechanisms of coeliac disease has uncovered principles that are relevant to other chronic inflammatory diseases.	★★★★
	Karell K, Louka AS, Moodie SJ, et al. "HLA types in celiac disease patients not carrying the DQA1*05–DQB1*02 (DQ2) heterodimer: results from the European Genetics Cluster on Celiac Disease" Genetic susceptibility to celiac disease is strongly associated with HLA-DQA1*05-DQB1*02 (DQ2) and HLA-DQA1*03-DQB1*0302 (DQ8). Study of the HLA associations in patients not carrying these heterodimers has been limited by the rarity of such patients. This European collaboration has provided a unique opportunity to study a large series of such patients. From 1008 European coeliac's, 61 were identified who neither carry the DQ2 nor DQ8 heterodimers. Fifty seven of these encoded half of the DQ2 heterodimer. The remaining 4 patients had a variety of clinical presentations. Three of them carried the DQA1*01-DQB*05 haplotype as did 20/61 of those carrying neither DQ2 nor DQ8. This may implicate a role of the DQA1*01-DQB*05 haplotype.	★★★★
	Hill ID, Dirks MH, Liptak GS, et al. "Guideline for the diagnosis and treatment of celiac disease in children: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition." The Celiac Disease Guideline Committee of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition has formulated a clinical practice guideline for the diagnosis and treatment of pediatric celiac disease based on an integration of a systematic review of the medical literature combined with expert opinion. The Committee examined the indications for testing, the value of serological tests, human leukocyte antigen (HLA) typing and histopathology and the treatment and monitoring of children with celiac disease. It is recommended that children and adolescents with symptoms of celiac disease or an increased risk for celiac disease have a blood test for antibody to tissue transglutaminase (TTG), that those with an elevated TTG be referred to a pediatric gastroenterologist for an intestinal biopsy and that those with the characteristics of celiac disease on intestinal histopathology be treated with a strict gluten-free diet.	★★★★
	Nadia Tinto et al. "High Frequency of Haplotype HLA-DQ7 in Celiac Disease Patients from South Italy" This study diagnosed CD in 666/5,535 individuals, 4.2% of whom were DQ2/DQ8-negative. Interestingly, DQ7 was one of the most abundant haplotypes in all CD patients and significantly more frequent in DQ2/DQ8-negative (38%) than in DQ2/DQ8-positive CD patients (24%) ($p<0.05$).	★★★★
	M. Araya et al. "DQ2, DQ7 and DQ8 Distribution and Clinical Manifestations in Celiac Cases and Their First-Degree Relatives" A total of 222 individuals were assessed (56 cases, 166 FDRs). 16.9% of FDRs were tTG positive; 53.6% of them showed overweight/obesity and 3% undernourishment; they spontaneously declared being asymptomatic, but detailed questioning revealed that 60.7% experienced symptoms, which had not been investigated. DQ2 was present in 53.9% and 43.9.0% of cases and FDRs ($p < 0.05$). The most frequent genotype distribution was DQ2/DQ7 (fr 0.392 (cases) and 0.248 (FDRs), respectively, $p < 0.02$). The next most common genotypes were HLA-DQ2/DQ8 (fr 0.236 in FDRs and 0.176 in cases, $p < 0.05$). 3.92% cases were not HLA-DQ2/DQ8 carriers.	★★★★

The complete list of references and the summary of performance studies can be found online at www.vibrant-wellness.com or BY CONTACTING CLIENT SERVICES AT +1(866)364-0963.

LAST NAME	FIRST NAME	GENDER	DATE OF BIRTH	ACCESSION ID	DATE OF SERVICE
VIBRANT AMERICA	DEMO	MALE	1996-11-29	1905130043	05-12-2019 09:43

Anemia	Current	Reference Range	Previous
Ferritin (ng/mL)	199	30~400	174 (04/13/2019)
Iron (ug/dL)	109	59~158	**164 H (04/13/2019)**
UIBC (µg/dL)	113	112~347	191 (04/13/2019)
TIBC (µg/dL)	222	171~505	355 (04/13/2019)
Transferrin (mg/dL)	**198 L**	203~362	**156 L (04/13/2019)**
Transferrin Saturation (%)	49	15~50	46 (04/13/2019)

Nutrition	Current	Reference Range	Previous
Folate (ng/mL)	>20.0	≥4.6	>20.0 (04/13/2019)
Vitamin D, 25-OH* (ng/mL)	**15.0 L**	30.0~108.0	**19.0 L (04/13/2019)**
Vitamin B12 (pg/mL)	**<150 L**	232~1245	**<150 L (04/13/2019)**

Comments

Likely vitamin D deficiency. Consider increasing vitamin D intake (e.g., adequate sun exposure and diet supplementation).; Associated with anemia, malnutrition, and malabsorption. Treat underlying cause.

	Test name	In Control	Moderate	High Risk	In Control Range	Moderate Range	High Risk Range	Previous
Dairy	Beta-Casein IgE* (kU/L)	<0.10			≤0.34	0.35~3.49	≥3.50	<0.10 04/13/2019
	Casomorphin IgE* (kU/L)	0.10			≤0.34	0.35~3.49	≥3.50	0.10 04/13/2019
	Cow's Milk IgE* (kU/L)	0.14			≤0.34	0.35~3.49	≥3.50	0.14 04/13/2019
	Goat's Milk IgE* (kU/L)	0.13			≤0.34	0.35~3.49	≥3.50	0.13 04/13/2019
	Whey Protein IgE* (kU/L)	0.11			≤0.34	0.35~3.49	≥3.50	0.11 04/13/2019