Vibrant Wellness | 1360 Bayport Ave, Ste B. San Carlos, CA 94070
1(866) 364-0963 | support@vibrant-wellness.com | www. vibrant-wellness.com

| | | | |
|---|---|---|---|
| **Final Report Date:** | 07-03-2018 18:31 | **Specimen Collected:** | 06-03-2018 18:31 |
| **Accession ID:** | 1512010000 | **Specimen Received:** | 06-03-2018 18:31 |

| LAST NAME | FIRST NAME | MIDDLE NAME | GENDER | DATE OF BIRTH | ACCESSION ID |
|---|---|---|---|---|---|
| TESTNAME | PATIENT | | MALE | 2008-08-24 | 1512010000 |

## PATIENT

Name: PATIENT TESTNAME
Date of Birth: 2008-08-24
Gender: Male
Age: 9
Height: 7'1" Weight: 169 lbs

Telephone #: 000-001-0002
Street Address: 1021 HOWARD AVENUE SUITE B
City: San Carlos
State: CA Zip #: 94070

Fasting: FASTING

## PROVIDER

Practice Name: Demo Client, MD
**Provider Name: Demo Client, MD (999994)**
Street Address: 1021 HOWARD AVENUE
City: SAN CARLOS
State: CA
Zip #: 94070
Telephone #: 800-842-7268
Fax #: 222-222-2222

**Vibrant Wellness** is pleased to present to you, **WheatZoomer** testing, to help you make healthy lifestyle choices in consultation with your physicians and dietitians. It is intended to be used as a tool to encourage a general state of health and well-being.

**WheatZoomer** is a wheat sensitivity analytics tool consisting of a microarray platform which has synthesized wheat proteins, as peptides, and offers very specific antibody-to-antigen recognition. The Vibrant Wheat Zoomer is designed to assess an individual's sensitivity to wheat. It also includes testing for the HLA isoforms associated with Celiac disease. The test provides nutritional guidance that can be discussed with your physician/dietitian.

**Interpretation of Report:** The test results of individual wheat proteins are calculated by comparing the average intensity of the peptides tested to the healthy reference range. Reference ranges have been established for pediatric and adult population using 192 healthy individuals. The reference range for each test populates automatically based on the age of each individual tested.

The results are displayed in 3 columns surrounded by GREEN (In Control), YELLOW (Moderate) or RED (High Risk) box. Potential risk, related information and potential risk mitigation choices are presented towards the end of the report and will populate for individual tests if you have a YELLOW or RED result.

**Ratings for the references** are calculated based on the Impact Factor, Citations, and Study Population of the references which correlate the antigen/antibody with the associated conditions. It is indicated based on a star based system (1 star – 5 stars) with 5 stars indicating the best correlation of the protein with the potential associated risk. The Impact Factor of the journal in which the reference is published is the number of citations received by articles published in that journal during the two preceding years, divided by the total number of articles published in that journal during the two preceding years. Study population includes the number of samples tested along with gender, age and ethnicity of the population.

Vibrant Wellness is a personalized health analytics company founded out of our passion to serve patients and providers. The Vibrant Wellness platform provides tools for you to track and analyze your general wellness profile. All testing offered by Vibrant Wellness is performed at a CLIA approved lab testing facility and licensed by California Department of Public Health.

Please Note - It is important that you discuss any modifications to your diet, exercise and nutritional supplementation with your physician before making any changes.

**To schedule an appointment with Vibrant Clinical Dietitians please call: Toll-Free 866-364-0963.**

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| LAST NAME | FIRST NAME | MIDDLE NAME | GENDER | DATE OF BIRTH | ACCESSION ID |
|---|---|---|---|---|---|
| TESTNAME | PATIENT | | MALE | 2008-08-24 | 1512010000 |

**Celiac HLA Genetics**

| HLA Type Tested | Results | Potential Risk |
|---|---|---|
| DQ2 | NEGATIVE | Patient is unlikely to develop celiac disease |
| DQ8 | NEGATIVE | |

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## 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 $\alpha^5$ and $\beta^2$ 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 $\alpha^5$ 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.

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## 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 | MIDDLE NAME | GENDER | DATE OF BIRTH | ACCESSION ID |
|---|---|---|---|---|---|
| TESTNAME | PATIENT | | MALE | 2008-08-24 | 1512010000 |

**Total Immunoglobulins**

| Test name | In Control | Moderate | High Risk | In Control Range | Moderate Range | High Risk Range | Previous |
|---|---|---|---|---|---|---|---|
| Total IgG (mg/dL) | 1061 | | | 462~1682 | | ≤461<br>≥1683 | 975<br>05/09/2018 |
| Total IgA (mg/dL) | | | 10 | 34~274 | | ≤33<br>≥275 | 78<br>05/09/2018 |

**Celiac**

| Test name | In Control | Moderate | High Risk | In Control Range | Moderate Range | High Risk Range | Previous |
|---|---|---|---|---|---|---|---|
| Transglutaminase 2 IgG | 0.46 | | | ≤0.94 | 0.95~1.05 | ≥1.06 | 0.75<br>05/09/2018 |
| Transglutaminase 2 IgA | | | 2.80 | ≤0.94 | 0.95~1.05 | ≥1.06 | 0.43<br>05/09/2018 |
| DGP IgG | | | 2.00 | ≤0.94 | 0.95~1.05 | ≥1.06 | 0.17<br>05/09/2018 |
| DGP IgA | | | 1.20 | ≤0.94 | 0.95~1.05 | ≥1.06 | 0.45<br>05/09/2018 |

**tTG/DGP Complex**

| Test name | In Control | Moderate | High Risk | In Control Range | Moderate Range | High Risk Range | Previous |
|---|---|---|---|---|---|---|---|
| tTG/DGP Fusion Peptide IgG | 0.16 | | | ≤0.89 | 0.90~1.10 | ≥1.11 | 0.50<br>05/09/2018 |
| tTG/DGP Fusion Peptide IgA | 0.85 | | | ≤0.89 | 0.90~1.10 | ≥1.11 | 0.40<br>05/09/2018 |

**Intestinal Permeability Panel**

| Test name | In Control | Moderate | High Risk | In Control Range | Moderate Range | High Risk Range | Previous |
|---|---|---|---|---|---|---|---|
| Zonulin (ng/mL) | <10.0 | | | ≤45.3 | 45.4~55.3 | ≥55.4 | 47.8<br>05/09/2018 |
| Anti-Zonulin IgG | 0.77 | | | ≤0.89 | 0.90~1.10 | ≥1.11 | 0.95<br>05/09/2018 |
| Anti-Zonulin IgA | 0.20 | | | ≤0.89 | 0.90~1.10 | ≥1.11 | 0.54<br>05/09/2018 |
| Anti-Actin IgG | 0.67 | | | ≤0.89 | 0.90~1.10 | ≥1.11 | 0.86<br>05/09/2018 |
| Anti-Actin IgA | 0.09 | | | ≤0.89 | 0.90~1.10 | ≥1.11 | 0.37<br>05/09/2018 |
| Anti-LPS IgA (U/ml) | 8.7 | | | ≤30.0 | | ≥30.1 | 61.0<br>05/09/2018 |
| Anti-LPS (IgG + IgM) (U/ml) | 125.9 | | | ≤281.0 | | ≥281.1 | 66.0<br>05/09/2018 |

| LAST NAME | FIRST NAME | MIDDLE NAME | GENDER | DATE OF BIRTH | ACCESSION ID |
|---|---|---|---|---|---|
| TESTNAME | PATIENT | | MALE | 2008-08-24 | 1512010000 |

**Transglutaminase Panel**

| Test name | In Control | Moderate | High Risk | In Control Range | Moderate Range | High Risk Range | Previous |
|---|---|---|---|---|---|---|---|
| Transglutaminase 3 IgG | 0.63 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.17 05/09/2018 |
| Transglutaminase 3 IgA | 0.42 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.18 05/09/2018 |
| Transglutaminase 6 IgG | 0.29 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.89 05/09/2018 |
| Transglutaminase 6 IgA | 0.23 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.44 05/09/2018 |

**Wheat Germ Panel**

| Test name | In Control | Moderate | High Risk | In Control Range | Moderate Range | High Risk Range | Previous |
|---|---|---|---|---|---|---|---|
| Wheat Germ Agglutinin IgG | 0.57 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.87 05/09/2018 |
| Wheat Germ Agglutinin IgA | 0.21 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.60 05/09/2018 |

**Gliadin Panel**

| Test name | In Control | Moderate | High Risk | In Control Range | Moderate Range | High Risk Range | Previous |
|---|---|---|---|---|---|---|---|
| Alpha Gliadin IgG | 0.79 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.64 05/09/2018 |
| Alpha Gliadin IgA | 0.39 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.63 05/09/2018 |
| Alpha-Beta Gliadin IgG | 0.40 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.36 05/09/2018 |
| Alpha-Beta Gliadin IgA | | 0.97 | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.51 05/09/2018 |
| Gamma Gliadin IgG | 0.41 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.75 05/09/2018 |
| Gamma Gliadin IgA | 0.34 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.59 05/09/2018 |
| Omega Gliadin IgG | 0.06 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.59 05/09/2018 |
| Omega Gliadin IgA | 0.62 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.65 05/09/2018 |
| Gluteomorphin IgG | 0.04 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.27 05/09/2018 |
| Gluteomorphin IgA | 0.43 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.50 05/09/2018 |
| Prodynorphin IgG | 0.12 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.39 05/09/2018 |
| Prodynorphin IgA | 0.02 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.32 05/09/2018 |

| LAST NAME | FIRST NAME | MIDDLE NAME | GENDER | DATE OF BIRTH | ACCESSION ID |
|---|---|---|---|---|---|
| TESTNAME | PATIENT | | MALE | 2008-08-24 | 1512010000 |

**Wheat Allergy Panel**

| Test name | In Control | Moderate | High Risk | In Control Range | Moderate Range | High Risk Range | Previous |
|---|---|---|---|---|---|---|---|
| Wheat Allergen IgE (kU/L) | <0.10 | | | ≤0.34 | 0.35~3.49 | ≥3.50 | <0.10 05/09/2018 |

**Glutenin Panel**

| Test name | In Control | Moderate | High Risk | In Control Range | Moderate Range | High Risk Range | Previous |
|---|---|---|---|---|---|---|---|
| HMW Glutenin IgG | | 0.90 | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.19 05/09/2018 |
| HMW Glutenin IgA | 0.25 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.62 05/09/2018 |
| LMW Glutenin IgG | 0.32 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.58 05/09/2018 |
| LMW Glutenin IgA | | 0.86 | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.62 05/09/2018 |

**Non-Gluten Wheat Panel**

| Test name | In Control | Moderate | High Risk | In Control Range | Moderate Range | High Risk Range | Previous |
|---|---|---|---|---|---|---|---|
| Serpin IgG | | 0.87 | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.73 05/09/2018 |
| Serpin IgA | 0.36 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.60 05/09/2018 |
| Farinins IgG | 0.18 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.46 05/09/2018 |
| Farinins IgA | 0.37 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.50 05/09/2018 |
| Amylase/Protease Inhibitors IgG | 0.01 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.70 05/09/2018 |
| Amylase/Protease Inhibitors IgA | | 0.99 | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.57 05/09/2018 |
| Globulins IgG | 0.58 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.75 05/09/2018 |
| Globulins IgA | 0.48 | | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.58 05/09/2018 |
| Purinin IgG | | 0.96 | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.86 05/09/2018 |
| Purinin IgA | | 0.87 | | ≤0.79 | 0.80~1.00 | ≥1.01 | 0.64 05/09/2018 |

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|---|---|---|---|---|---|
| TESTNAME | PATIENT | | MALE | 2008-08-24 | 1512010000 |

Comments

## Celiac

### *Potential Risk:*

Increased levels of DGP IgA could be suggestive of celiac disease or other gluten-sensitive enteropathies as per AGA guidelines.;

Increased levels of DGP IgG could suggest sensitivity to deamidated gliadins.;

Antibodies to TG2 is associated with celiac disease or other gluten-sensitive enteropathies as per AGA guidelines.

### *Related Information:*

Deamidated gliadin is produced by acid or enzymatic treatment of gluten. The enzyme tissue transglutaminase converts some of the abundant glutamines to glutamic acid. This is done because gliadins are soluble in alcohol and cannot be mixed with other foods without changing the foods' qualities. The cellular immunity to deamidated gliadin is much greater than native gliadin and increased levels of DGP IgG can result in symptomatic gluten-sensitive enteropathy.;

Transglutaminases are enzymes found within the body and immune reactions to transglutaminase indicates the presence of an autoimmune condition.

### *Potential Risk Mitigation Choices:*

**Consider being on a strict gluten free diet.;**

**Consider going on a gluten free diet.**

| LAST NAME | FIRST NAME | MIDDLE NAME | GENDER | DATE OF BIRTH | ACCESSION ID |
|---|---|---|---|---|---|
| TESTNAME | PATIENT | | MALE | 2008-08-24 | 1512010000 |

Comments

## Gliadin Panel

### *Potential Risk:*

Increased levels of Beta Gliadin IgG/IgA could suggest sensitivity to the beta gliadin component of gluten.

### *Related Information:*

Gliadin constitutes a class of proteins that are present in wheat and other cereal which give it the ability to rise properly when baked. The main types of gliadin are alpha, beta, gamma and omega gliadins. Research has suggested that antibody reactivity against all the above mentioned forms of gliadin are found in individuals with 'Wheat related disorders.'

### *Potential Risk Mitigation Choices:*

**Consider going on a gluten free diet.**

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| LAST NAME | FIRST NAME | MIDDLE NAME | GENDER | DATE OF BIRTH | ACCESSION ID |
|---|---|---|---|---|---|
| TESTNAME | PATIENT | | MALE | 2008-08-24 | 1512010000 |

Comments

## Glutenin Panel

### *Potential Risk:*

Elevated levels of LMW Glutenin has been associated with Wheat Sensitivity, asthma, Atopic dermatitis, Urticaria and Anaphylaxis.;

Elevated levels of HMW Glutenin has been associated with Wheat Sensitivity, asthma and Atopic dermatitis.

### *Potential Risk Mitigation Choices:*

**Consider avoiding wheat in your diet.;**

**Consider going on a gluten free diet.**

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| LAST NAME | FIRST NAME | MIDDLE NAME | GENDER | DATE OF BIRTH | ACCESSION ID |
|---|---|---|---|---|---|
| TESTNAME | PATIENT | | MALE | 2008-08-24 | 1512010000 |

Comments

## Non-Gluten Wheat Panel

### *Potential Risk:*

Increased levels of antibodies to non-gluten wheat proteins (serpins, purinins, farinins, amylase/protease inhibitors and globulins) are responsible for inflammation in patients with wheat sensitive enteropathies.

### *Related Information:*

Non-gluten proteins constitute about 25% of the total protein content of wheat cereal. Recently it has been shown that these non-gluten proteins are immune-reactive in individuals with wheat sensitivity. The 5 groups of non-gluten proteins which are distinctly different from the gluten proteins that are responsible for inflammation in patients with wheat sensitivity are serpins, purinins, farinins, amylase/protease inhibitors and globulins.

### *Potential Risk Mitigation Choices:*

**Consider avoiding wheat in your diet.**

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## What is Gluten?

Gluten is a name for a group of proteins found in wheat, rye, barley and triticale. It acts as a 'glue' to give grains their doughy texture and is also commonly used as a food additive or thickener.

## How to Eliminate Gluten Step-by-Step

If you have been instructed to go on a gluten-free diet, you might feel overwhelmed with how exactly to eliminate gluten 100% from your diet. Follow these steps to make your transition as smooth as possible:

1. Work with your Vibrant Registered Dietitian Nutritionist to develop a custom plan to replace gluten-containing foods you may already be consuming regularly.
2. Learn what foods naturally contain gluten
3. Learn what foods commonly have gluten added to them
4. Learn what foods might contain hidden sources of gluten
5. Learn to read labels to identify gluten-free foods (consider using a smartphone app)
6. Learn practical strategies to avoid cross contamination

## Tips for Dining Out

- Be prepared and research the menu online before you arrive
- Explain your gluten-free needs to your server
- Ask detailed questions about how your food will be prepared (Are separate utensils used? Are separate preparation surfaces used? Etc)
- A number of apps exist that identify restaurants that cater to gluten-free patrons

### Additional Resources

Celiac Disease Foundation www.celiac.org
Beyond Celiac (National Foundation of Celiac Awareness) www.beyondceliac.org
The Gluten Intolerance Group of North America www.gluten.org

## Gluten vs. Wheat…What's the Difference?

Gluten is a protein that is found in wheat, rye and barley. Wheat is a cereal grain that contains both gluten and non-gluten proteins. Most gluten free foods are wheat free but some may contain traces of wheat proteins.

| Foods that contain gluten or might contain gluten* | Foods that are naturally gluten free* |
|---|---|
| Wheat and wheat products (farina, kamut, semolina, spelt, baked goods such as bread, cakes, cookies, granola bars, pasta and other sweets) | Animal proteins: beef, chicken, pork, fish, shellfish and wild game; eggs, yogurt, kefir, cottage cheese, milk (cow or goat) |
| Rye products and beer or ale made from rye | All fresh fruits |
| Seasoning blends, sauce mixes, gravies and dressings | All fresh vegetables |
| Soups and marinades | Pure herbs or spices (basil, cumin, oregano, etc) |
| Barley products and beer or ale made from barley, malt products such as malt vinegar, malted milk, malt flavor | Non-gluten grains: amaranth, buckwheat, rice, quinoa, gluten-free oats, sorghum |
| Soy sauce and teriyaki sauce | Legumes (beans) |
| Energy bars, trail mix, wheatgrass, cereals, oats (unless they say certified gluten-free) | Oils: coconut oil, extra virgin olive oil, avocado oil |
| Breaded foods, meatballs, veggie burgers, deli meat, cold cuts, imitation crab | Nuts: almonds, walnuts, peanuts, cashews, pistachios, Brazil nuts |
| Prescription and over-the-counter medications and supplements | Stevia and dark chocolate (70% or more cocoa) |
| Cosmetic products and skincare products | Wine |

***naturally gluten-free foods may have gluten-containing ingredients added to them during processing, therefore it is always recommended to read labels before consuming**

## Glossary

**Farinins** - The name "Farinins" was given for avenin-like proteins because they are slightly closer in primary structure to gamma-gliadins than to avenins.

**Gliadin** constitutes a class of proteins that are present in wheat and other cereal which give it the ability to rise properly when baked. The main types of gliadin are alpha, gamma and omega gliadins. Most commercial ELISA plates focus only on the alpha/gamma gliadin component and its deamidated forms. Research has however shown that antibody reactivity against all the 3 main forms of gliadin are found in individuals with 'Wheat related disorders'. The Vibrant Wheat Zoomer covers all known gliadins from all the different wheat species in both native and deamidated form making it the most comprehensive test against gliadins. The Vibrant Wheat Zoomer also includes all the key gliadin motifs– 33mer alpha gliadin, 26mer gamma gliadin, 17mer omega gliadin.

**Globulins** - Several types of Globulins are also detected among the flour proteins. Proteins termed globulin-1 or alpha-globulin are encoded at the highly conserved Glo-2 locus between the loci for the x- and y-type HMW-GS on chromosome 1.

**Glutenin** is a major protein found in wheat and constitutes about 47% of its protein content. Glutenin is responsible for the strength and elasticity of dough. The main types of glutenin are the LMW (low molecular weight) and the HMW (high molecular weight) glutenin. HMW glutenin has been associated with Celiac disease, asthma and Atopic dermatitis. LMW Glutenin has been associated with Celiac disease, asthma, Atopic dermatitis, Urticaria and Anaphylaxis.

**Gluteomorphin** is an opioid peptide that is formed during digestion of the gliadin component of the gluten protein.

**Intestinal Permeability** is a term describing the control of material passing from inside the gastrointestinal tract through the cells lining the gut wall, into the rest of the body. One way in which intestinal permeability is modulated is via CXCR3 receptors in cells in the intestinal epithelium, which respond to zonulin. Gliadin (a glycoprotein present in wheat) activates zonulin signaling irrespective of the genetic expression of autoimmunity, leading to increased intestinal permeability to macromolecules. The cytoskeleton is also made up of proteins, which comprise a network of thin, overlapping fibers known as the actin-myosin network. This partnership between the actin-myosin network proteins controls the permeability of the tight junctions, and thus the intestinal barrier.

**Lipopolysaccharides (LPS)** are a naturally occurring endotoxin found in the gut, genitourinal, and respiratory tracts. A healthy mucosal layer with intact tight junctions prevents the paracellular translocation of LPS. The presence of LPS antibodies in the blood has been discovered to be clinically relevant when attempting to identify the degree of intestinal barrier permeability.

**Non Gluten Wheat Proteins** Gliadins and Glutenins comprise approximately 70 different proteins and constitute about 75% of the total protein content of wheat cereal. The key proteins identified to be immune-reactive include Serpins, farinins, globulins, and amylase/protease inhibitors.

**Prodynorphin** is an opioid that is a basic building block of endorphins.

**Purinin** proteins are legumin-like 12 S globulin storage proteins encoded at Tri-A1 and Tri-D1 on the short arms of chromosomes 1A and 1D. The native proteins exist as hetero-tetramers composed of long and short arms from two cleaved, disulfide-linked triticin precursors.

**Serpins** are serine protease inhibitors and the wheat serpins are suicide substrate inhibitors of chymotrypsin and cathepsin A that may serve to inactivate serine proteases of grain-boring insects.

**Transglutaminases** – 2, 3 and 6 Transglutaminases are enzymes that catalyze an isopeptide bond formation between a free amine group and the acyl group. The Vibrant Wheat Zoomer includes transglutaminases 2, 3 and 6 which are known to be associated with various disease conditions. **Tissue transglutaminase or transglutaminase 2** IgA and IgG profile is one of the most important tests in the diagnostics of celiac disease. tTG is a known autoantigen in celiac disease which has replaced the tissue level tests like antiendomysium antibody test. Clinically tTG has been determined to have a strong sensitivity (99%) and specificity (90%) for identifying celiac disease. While Wheat sensitivity in many cases presents itself as celiac disease in some individuals it is associated with dermatitis herpetiformis. Serum from patients with dermatitis herpetiformis has shown an increased binding towards **transglutaminase 3** or epidermal transglutaminase. Gluten sensitivity is sometimes also associated with neurological disorders. This condition also known as gluten ataxia occurs in around 10% of the patients with gluten sensitivity. These patients have been found to have developed antibodies against a different transglutaminase namely **transglutaminase 6**.

**tTG/DGP Complex** – tTG/DGP complex comprises of a synthesized peptide which contains a portion of the tTG region and a portion of the DGP region. Recent studies support the hypothesis that a neoepitope may be formed in CD patients' sera under in vivo physiological conditions, by a covalent cross-link between tTG and deamidated gliadin peptides, and this neo-antigen may be specifically recognized by autoantibodies. The tTG/DGP complex could potentially indicate the healing status of celiac disease.

**Wheat alpha-amylase and protease inhibitors** are reported to be active against the amylases and proteases from insects such as grain-boring weevils. However, they also are sufficiently abundant to serve as storage proteins for the developing grain and are a source of essential amino acids such as Lys, Met and Cys for humans who consume wheat products.

**Wheat Germ Agglutenin** Wheat germ agglutinin is a lectin that protects wheat from bacteria, yeast and insects and is naturally found in all wheat varieties. The Vibrant Wheat Zoomer includes the different agglutinins from both T.aestivum and T.urartu varieties. Lectins have the capacity to bind to different cell types and are also resistant to digestive enzymes making them a possible candidate for immune-sensitivity. Wheat Germ Agglutinin (WGA) irritates and causes premature cell death in the gut and has been known to lead to a leaky gut condition. WGA also disrupts the mucus membrane in the gut, which can cause bacterial overgrowth and lead to a host of digestive issues like GERD and ulcers.

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## References

| PANEL | REFERENCE/ABSTRACT | RATING |
|---|---|---|
| LEAKY GUT PANEL | **Alessio Fasano.Zonulin and Its Regulation of Intestinal Barrier Function: The Biological Door to Inflammation, Autoimmunity, and Cancer.** This review talks about the increased interest in the role of a "leaky gut" in the pathogenesis of several pathological conditions targeting both the intestine and extra intestinal organs. | ★★★★★ |
| | **Silvia Pedreira et.al. Significance of smooth muscle/anti-actin autoantibodies in celiac disease.** The study evaluates the clinical relevance of the presence of IgA type anti-actin antibody (AAA) and SMA in 92 adult patient with celiac disease. The results indicted the presence of increased IgA AAA serum levels is a highly sensitive marker of the disturbed architecture of intestinal epithelial cells of CD patients also the presence of SMA seems to define a distinct subset of CD patients with a more severe clinical outcome. | ★★★ |
| | **Melanie Uhde, Mary et. al. Intestinal cell damage and systemic immune activation in individuals reporting sensitivity to wheat in the absence of coeliac disease.** The study aims to determine if sensitivity to wheat in the absence of coeliac disease is associated with systemic immune activation that may be linked to an enteropathy. | ★★★★ |
| WHEAT GERM PANEL | **Karin de Punder and Leo Pruimboom. The Dietary Intake of Wheat and other Cereal Grains and Their Role in Inflammation.** This review states the evidence from in vitro, in vivo and human intervention studies that describe how the consumption of wheat, other cereal grains, can contribute to the manifestation of chronic inflammation and autoimmune diseases by increasing intestinal permeability and initiating a pro-inflammatory immune response. | ★★★ |
| | **L M Sollid, J Kolberg, H Scott, J Ek, O Fausa, and P Brandtzaeg. Antibodies to wheat germ agglutinin in coeliac disease.** The study shows the celiac patients have significantly higher Serum IgG and IgA antibodies to wheat germ agglutinin (WGA) compared to the control group. Thus adding WGA as a potential biomarker for pathogenesis of CD. | ★★ |
| GLIADIN PANEL | **Alessio Fasano.Zonulin and Its Regulation of Intestinal Barrier Function: The Biological Door to Inflammation, Autoimmunity, and Cancer.** This review talks about the increased interest in the role of a "leaky gut" in the pathogenesis of several pathological conditions targeting both the intestine and extra intestinal organs. | ★★★★★ |
| | **Luca Elli, Federica Branchi, Carolina Tomba, Danilo Villalta, Lorenzo Norsa, Francesca Ferretti, Leda Roncoroni, and Maria Teresa Bardella. Diagnosis of gluten related disorders: Celiac disease, wheat allergy and non-celiac gluten sensitivity.** The review article covers a complete overview of celiac disease, wheat allergy and non-celiac gluten sensitivity and its current clinical diagnosis. | ★★ |
| | **Chirdo FG, Rumbo M, Carabajal P, Mavromatópulos E, Castagnino N, Añón MC, Fossati CA. Determination of anti--gliadin antibodies in serologic tests for coeliac disease.** The study compromised of 105 coeliac patients, 81 healthy controls, and 73 subjects in a disease control group to evaluate the efficacy of omega-gliadins to be a useful antigen in serologic detection of coeliac disease. | ★★★ |
| | **Aristo Vojdani .The Characterization of the Repertoire of Wheat Antigens and Peptides Involved in the Humoral Immune Responses in Patients with Gluten Sensitivity and Crohn's Disease.** The study examines the humoral immune response to various wheat proteins and peptides in patients with gluten sensitivity or Crohn's disease. In gluten-sensitive patients, IgG reacted most against transglutaminase, prodynorphin, wheat extract, and -, -, and -gliadin; IgA reacted most against wheat then transglutaminase, glutenin, and other peptides. In Crohn's disease patients, IgG reacted most against wheat and wheat germ agglutinin then transglutaminase, prodynorphin, -, and -gliadin; IgA reacted foremost against prodynorphin then transglutaminase and -gliadin. | ★★ |
| GLUTENIN PANEL | **G Salcedo, S Quirce, A Diaz-Perales. Wheat Allergens Associated with Baker's Asthma.** This review deals with the current diagnosis and immunomodulatory treatments, as well as the role of wheat allergens as molecular tools to enhance management and knowledge of Baker's Astma. | ★★★ |
| | **Frances M Dupont et.al. Deciphering the complexities of the wheat flour proteome using quantitative two-dimensional electrophoresis, three proteases and tandem mass spectrometry.** The study of wheat genome to identify the majority of abundant flour proteins for a single wheat cultivar, relate them to individual gene sequences and estimate their relative levels. | ★★★ |
| NON GLUTEN WHEAT PANEL | **Sina Huebener et. al. Specific Nongluten Proteins of Wheat are Novel Target Antigens in Celiac Disease Humoral Response.** The study aims to investigate the level and molecular specificity of antibody response to wheat non gluten proteins in celiac disease. The results demonstrate that, in addition to the well-recognized immune reaction to gluten, celiac disease is associated with a robust humoral response directed at a specific subset of the no gluten proteins of wheat. | ★★★ |
| TRANSGLUTAMINASE PANEL | **Timo Reunala, Teea T. Salmi and Kaisa Hervonen. Dermatitis Herpetiformis: Pathognomonic Transglutaminase IgA Deposits in the Skin and Excellent Prognosis on a Gluten-free Diet.** The study shows the coeliac disease in the gut appears to be a result of the IgA Epidermal transglutaminase antibody complexes aggregated into DH skin. | ★★ |
| | **Hull CM, Liddle M, Hansen N, Meyer LJ, Schmidt L, Taylor T, Jaskowski TD, Hill HR, Zone JJ. Elevation of IgA anti-epidermal transglutaminase antibodies in dermatitis herpetiformis.** The study to determine the association between Dermatitis herpetiformis with IgA antibodies against TG2 and TG3. The results indicates IgA antibodies to TG3 are elevated in patients with DH and adults with Celiac disease. | ★★★ |
| | **Gadoth A, Nefussy B, Bleiberg M, Klein T, Artman I, Drory VE. Transglutaminase 6 Antibodies in the Serum of Patients with Amyotrophic Lateral Sclerosis.** The Study to evaluate the prevalence of celiac disease-related antibodies and HLA antigen alleles, as well as TG6 antibodies, in patients with amyotrophic lateral sclerosis (ALS) and healthy individuals serving as controls to determine whether a neurologic presentation of a gluten-related disorder mimicking ALS might occur in some patients. The result indicates certain cases, an ALS syndrome might be associated with autoimmunity and gluten sensitivity and also study indicates gluten sensitivity is potentially treatable with strict gluten free diet. | ★★★★★ |
| tTG/DGP Complex Panel | **Margherita Di Pisa et.al. Synthetic Peptides Reproducing Tissue TransglutaminaseGliadin Complex Neo-epitopes as Probes for Antibody Detection in Celiac Disease Patients' Sera.** Sera from 48 CD patients were collected at the diagnosis before gluten-free diet (39 females, 9 males; age range 2.252 years). Two of 48 (4%) CD patients presented IgA deficiency. Analysis of patients' subgroups established a possible clinical correlation not detected by established tests. These observations indicate that a neoepitope may be formed in CD patients' sera under in vivo physiological conditions, by a covalent cross-link between tTG and deamidated gliadin peptides, and this neo-antigen may be specifically recognized by autoantibodies. | ★★★★ |

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.

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## Test Risk and Limitations

Wheat Zoomer testing is performed at Vibrant America, a CLIA certified laboratory, and utilizes ISO-13485 developed technology. However, laboratory error can occur, which might lead to incorrect results. Some of them may include sample mislabeling or contamination, operational error or failure to obtain data for certain proteins. Vibrant's laboratory may need a second sample to complete the testing.

Vibrant America has effective procedures in place to protect against technical and operational problems. However, such problems may still occur. Examples include failure to obtain the result for a specific protein due to circumstances beyond Vibrant's control. Vibrant may re-test a sample in order to obtain these results but upon re-testing the results may still not be obtained. As with all medical laboratory testing, there is a small chance that the laboratory could report incorrect results. A tested individual may wish to pursue further testing to verify any results.

Tested individuals should not change their diet, physical activity, or any medical treatments they are currently using based on genetic testing results without consulting their personal health care provider. These risk factors for Wheat Zoomer are based on selected peer reviewed scientific research findings as listed under references.

Tested individuals may find their experience is not consistent with Vibrant's selected peer reviewed scientific research findings of relative improvement for study groups. The science in this area is still developing and many personal health factors affect diet and health. Since subjects in the scientific studies referenced in this report may have had personal health and other factors different from those of tested individuals, results from these studies may not be representative of the results experienced by tested individuals. Further, some recommendations may or may not be attainable, depending on the tested individuals' physical ability or other personal health factors.

A limitation of this testing is that most scientific studies have been performed in Caucasian populations only. The interpretations and recommendations are done in the context of Caucasian studies, but the results may or may not be relevant to tested individuals of different or mixed ethnicities. Interference studies have not been established for individuals on immunosuppressive drugs.

Based on test results and other medical knowledge of the tested individual, health care providers might consider additional independent testing, or consult another health care provider or genetic counselor.