

PROMETHEUS® **Celiac PLUS**

Serology. Genetics. Answers.

Now you can complete  
the picture

**GENETICS**  
What is their risk?

**SEROLOGY**  
Do they have it?



When diagnosing celiac disease...  
**Now you can complete the picture**

**PROMETHEUS® Celiac PLUS**

Serology. Genetics. Answers.

## Celiac tends to be underdiagnosed<sup>1,2</sup>

**≈ 3 million**

people in the United States are estimated to have celiac disease<sup>3</sup>

**11 years**

is the average time that patients experience symptoms before being diagnosed with celiac disease<sup>4</sup>

**> 50%**

of patients who are diagnosed with celiac disease do not present with diarrhea<sup>5</sup>

**16% savings**

in mean medical costs: months 12-24 post-diagnosis vs 12 months pre-diagnosis in a US study of 10.2 million patients<sup>6</sup>

### Other pathologies may make accurate diagnosis even more difficult

Gastrointestinal Manifestations <sup>3</sup>	Extraintestinal Manifestations <sup>3</sup>	Populations at Higher Risk <sup>3</sup>
Diarrhea	Dermatitis herpetiformis	Type 1 diabetes mellitus
Weight loss	Iron deficiency anemia	First- and second-degree relatives
Failure to grow	Short stature	Turner syndrome
Bloating and distension	Delayed puberty	Down syndrome
Anorexia	Infertility	Williams syndrome
Constipation	Osteoporosis	Other
Other	Vitamin deficiencies	
	Other	

## Only PROMETHEUS® Celiac PLUS combines serology and genetics in one comprehensive test

### Reliable answers to help put your patients on an appropriate path

- Early detection may help you optimize therapeutic outcomes
- One blood draw helps identify disease and stratify risk
- Clear risk stratification may enable you to prevent disease onset
- Rule out celiac disease for life<sup>7</sup>

### More information than other diagnostic alternatives<sup>5,b</sup>

Ambiguities in testing	Possible Effects	How Celiac PLUS may help	Celiac Genetics	Celiac Serology	Celiac PLUS
Interlaboratory variability in test results	False-negative results	Standardized tests through consistent team of technicians	✓	✓	✓
Partial villous atrophy	Negative EMA, tTG, or both	HLA-DQ2 and HLA-DQ8 testing are included. DGP-IgA also included in panel	✓	✓	✓
Testing for only EMA or tTG	Miss potential celiac patients	Both EMA and tTG are included		✓	✓
Low gluten intake by patient	Negative serologies	HLA-DQ2 and HLA-DQ8 testing are included	✓		✓
Use of immunosuppressants	Negative serologies	HLA-DQ2 and HLA-DQ8 testing are included	✓		✓
Selective IgA deficiency	Negative IgA may mean false negative EMA and tTG	Shows results of DGP-IgG antibody and total IgA level		✓	✓
Questionable diagnosis of celiac disease	Unclear on how to advise patient	Order the most comprehensive tests	✓	✓	✓

<sup>b</sup> Adapted from Green et al, 2003.



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## PROMETHEUS® Celiac Genetics The only test that quantifies the risk for every patient

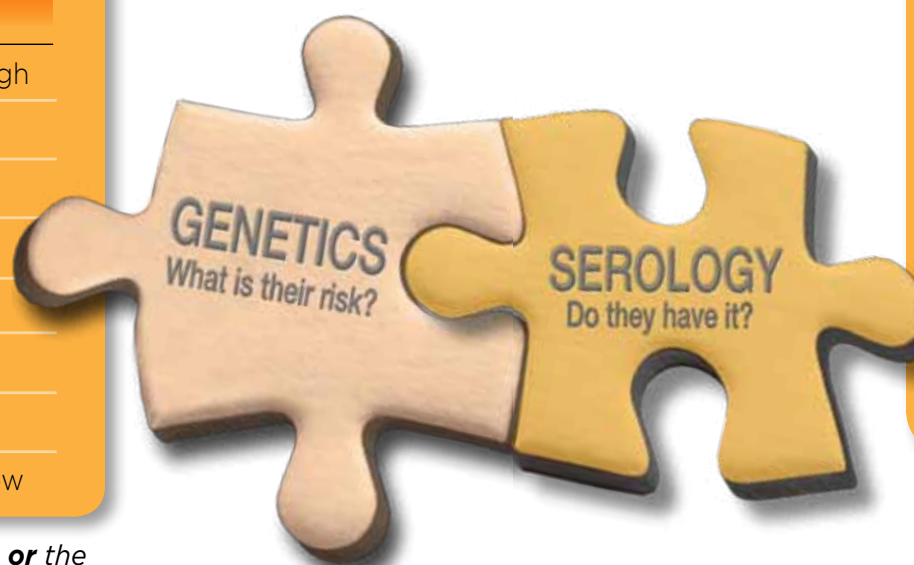
## PROMETHEUS® Celiac Genetics Detects disease by providing serologic answers

While other genetic tests for celiac disease put all at-risk patients in the same undifferentiated categories, *only* Prometheus genetic testing quantifies the *specific risk for every patient* based on proven genetic patterns\*

Category Number	DQ Genotype Category	Increased Risk <sup>8,9,10</sup>	Relative Risk
8	DQ2 homozygous	31x	Extremely high
7	DQ2/other high-risk gene	16x	Very high
6	DQ2/DQ8	14x	Very high
5	DQ8 homozygous	10x	High
4	DQ2 heterozygous	10x	High
3	DQ8 heterozygous	2x	Moderate
2	DQ2/other low-risk gene	< 1x	Low
1	DQ2-, DQ8-	< 0.1x	Extremely low

Genetics  
quantifies  
risk

Serology  
detects  
disease



PROMETHEUS® Celiac Serology	
Serology Marker	Test Advantages
hu tTG-IgA	Human recombinant tTG-IgA provides high sensitivity and specificity <sup>12</sup>
EMA-IgA	Highest specificity marker <sup>12</sup>
Total serum IgA	Helps identify a subset of IgA-deficient celiac patients who could be missed without it <sup>5</sup>
DGP IgG	Identification of IgA deficiency and positive IgG suggest a need for biopsy <sup>5</sup>
DGP IgA	Celiac disease is associated with selective IgA deficiency <sup>13</sup>

Most celiac patients carry **either** the DQ2 haplotype (about 95% of celiac patients) **or** the DQ8 haplotype (about 5% of celiac patients). **Specific combinations may confer different risks** for the development of celiac disease, as shown above.<sup>9</sup>

\*Risk stratification model is verified in a study based on the largest DNA analysis of at-risk patients (N = 10,191).<sup>11</sup>

### More information for a better diagnosis

- Approximately 40% of US adults have genes associated with celiac disease<sup>3</sup>
- Other genetic tests for celiac disease only provide a simple “yes” or “no” answer
- A negative predictive value (NPV) of > 99.5% allows you to rule out celiac disease for life<sup>11</sup>

### Different from other celiac serology tests

- Single-marker tests may miss 20% of cases<sup>5</sup>
- Combines important serologic markers for diagnosing celiac disease
- Determination of antibodies against deamidated gliadin peptides (DGP) has high diagnostic accuracy<sup>13</sup>
- Reliable and consistent results from a recognized leader in celiac testing with one team of technicians (no interlaboratory variability)



When diagnosing celiac disease...  
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## PROMETHEUS® Celiac PLUS test reports show complete information at a glance

**SAMPLE REPORT**  
**PROMETHEUS® Celiac PLUS**  
Comprehensive Celiac Evaluation (Serology and Genetics)

9410 Carroll Park Drive  
San Diego CA 92121  
Toll Free: 888-423-5227  
www.prometheuslabs.com

Patient & Order Information				Report Recipient	
Order ID	2182008			Undefined Physician M.D.	
Patient	Test, Patient			Prometheus Laboratories Inc.	
DOB	01/01/1950			9410 Carroll Park Drive	
SSN	Sex	X	Prometheus ID	San Diego, CA 92121	
Institution ID	1473852			858/824-0805	Phone 858/332-3346
Ordered	05/26/2011	Completed	05/26/2011		
Ordered By	Undefined Physician M.D.				
ICD9 Codes	789			Institution Sample ID:	
Sample ID: ST10526003	Collection Date:	05/25/2011 10:16PM	(Serum)	Institution Sample ID:	
Sample ID: ST10526004	Collection Date:	05/25/2011 10:15PM	(Whole Blood)		

**Summary Interpretation**  
Celiac Disease Highly Unlikely

IgG serological marker for celiac disease detected.

Positive DGP. IgG may also occur in normal individuals as well as in other GI conditions.

Assay Name	Result	Reference Range
Deamidated Gliadin Peptide Antibody, IgG (DGP IgG)	4.8 EU/ml +	< 4.9 EU/ml
Deamidated Gliadin Peptide Antibody, IgA (DGP IgA)	0.6 EU/ml -	< 6.1 EU/ml
Anti-Human Tissue Transglutaminase IgA ELISA (TTG IgA)	0.2 U/ml -	<10.3 U/ml
Anti-Endomysial IgA IFA (EMA IgA)	Negative	Negative
Total Serum IgA by Nephelometry (TOTAL IgA)	70 mg/dl	< 3 years: 8-228 mg/dl, 3-13 Years: 41-295 mg/dl, > 13 years to adult: 44-441 mg/dl

**Celiac Risk Genes Not Detected.**

Category #	DQ Genotype	Increased Risk	Relative Risk
1	DQ2-, DQ8-	<0.1X	EXTREMELY LOW

**Over all Risk for Patients Carrying the DQ Genotype**

Category #	DQ Genotype	Increased Risk	Relative Risk
8	DQ2 Homozygous	31X	EXTREMELY HIGH
7	DQ2/other high risk gene	15X	VERY HIGH
6	DQ2/DQ8	10X	HIGH
5	DQ8 Homozygous	10X	HIGH
4	DQ2 heterozygous	2X	MODERATE
3	DQ8 heterozygous	<1X	LOW
2	DQ2/other low risk gene	<0.1X	EXTREMELY LOW
1	DQ2-, DQ8-	<0.1X	EXTREMELY LOW

Most celiac patients carry either the DQ2 (about 95% of celiac) or the DQ8 haplotype (about 5% of celiac). There are two DQ2 haplotypes, but only one DQ8 haplotype. Specific combinations may confer different risks for the development of celiac disease, as shown above(7). 1) Pletzka M, et al. Stratifying Risk for Celiac Disease in a Large At-Risk United States Population by Using HLA Alleles. Clin Gastroenterol Hepatol. 2009; 7:966-971. 2) Fasano A, Bertl I, et al. Prevalence of celiac disease in at-risk and not-at-risk groups in the United States: a large multicenter study. Arch Intern Med. 2003; 163: 288-292. 3) Koning F, Schuppan D, Cerf-Bennussan N, Solid LM. Pathomechanisms in celiac disease. Best Pract Res Clin Gastroenterol. 2005; 19: 373-387.

Res Clin Gastroenterol. 2005; 19: 373-387. Information regarding genetic counseling is available through our website at www.prometheuslabs.com. The methodology for this test was reviewed by the Laboratory Medical Director. InnoGenetics, high-resolution sequence specific oligonucleotide (SSOP) with 2 separate multiplexed PCR amplifications and 72 probe hybridizations for the detection of HLA DQ2/DQ8 allelic variants. This test was developed and its performance characteristics determined by Prometheus Laboratories Inc. It has not been cleared or approved by the U.S. Food and Drug Administration.

Prometheus diagnostic services provide important information to aid in the diagnosis and management of certain diseases. Test results should be used with other clinical and diagnostic findings to make a diagnosis and prognosis. This test may be covered by one or more US pending or issued patents - see prometheuslabs.com for details.

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Prometheus Laboratories Inc. is a CAP-accredited CLIA laboratory.

Summary information

Serology results: Do they have it?

Genetic results: What is their risk?

PROMETHEUS® Celiac PLUS  
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## Ordering PROMETHEUS® Celiac PLUS is straightforward

- Ask your local Prometheus representative for more information about in-network laboratories in your area
- When you are ready, contact your Prometheus representative to order your free transportation kit and test requisition form
- For more information or to order directly, call **Prometheus Client Services at 888-423-5227**



PROMETHEUS® Celiac PLUS

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## PROMETHEUS® Celiac PLUS

- The only diagnostic test that uses a single blood draw for combined serologic and genetic celiac disease testing
- The only diagnostic test that stratifies future risk of celiac disease
- A comprehensive diagnostic test from a recognized leader in celiac testing
- Reliable and consistent results from a laboratory with experience analyzing greater than 100,000 celiac disease tests—so there's less room for doubt

For more information or to order directly,  
call Prometheus Client Services at

**888-423-5227**  
Fax to **858-824-0896**

PROMETHEUS® Celiac PLUS consists of PROMETHEUS® Celiac Serology and PROMETHEUS® Celiac Genetics, which can be ordered separately.

Prometheus diagnostic services provide important information to aid in the diagnosis and management of certain diseases and conditions. How this information is used to guide patient care is the responsibility of the physician.

For electronic test results, where and when you need them. 

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Therapeutics & Diagnostics

For the person in every patient®

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