



LAB #: F000000-0000-0  
PATIENT: Sample Patient  
ID: P00000000  
SEX: M  
DOB: AGE: 55

CLIENT #: 12345  
DOCTOR:  
Doctor's Data, Inc.  
3755 Illinois Ave.  
St. Charles, IL 60174 U.S.A.

## Zonulin; stool

	RESULT / UNIT	REFERENCE INTERVAL	REFERENCE INTERVAL		
			LOW	MOD	HIGH
Zonulin*	82.3 ng/mL	< 80.0			

The level of the fecal zonulin antigen is a clinically useful marker of intestinal permeability of the intestinal epithelium. Zonulin is a protein that reversibly regulates paracellular intestinal permeability; it is made in intestinal enterocytes and liver cells. High levels of zonulin are associated with increased intestinal permeability because it induces breakdown of the tight intercellular junctions between epithelial cells. Several autoimmune, inflammatory and neoplastic diseases have been associated with elevated levels of zonulin, or evidence of increased intestinal permeability. Chronically elevated serum zonulin levels have been associated with celiac disease and non-celiac gluten sensitivity, Metabolic syndrome, obesity, type I diabetes, juvenile nonalcoholic fatty liver disease, Crohn's disease, Lichen planus and possibly, food sensitivities, multiple sclerosis, rheumatoid arthritis, asthma and inflammatory bowel disease. Recently elevated fecal zonulin levels have been reported for adult patients with Metabolic syndrome, Crohn's disease and apparently healthy cigarette smokers. Elevated serum levels of zonulin have been correlated with results from the established lactulose mannitol test, but to date no such correlation has been reported with fecal zonulin.

Cellular receptors for zonulin are present in the small and large intestines, the heart and the brain. Zonulin release from the intestinal mucosa may be triggered by gliadin fragments, direct adherence of any bacteria to the apical surface of intestinal epithelial cells, excessive bacteria-derived LPS, bacterial enterotoxins / proteases, corticosteroids, and other dietary protein fragments. Excessive intake of simple sugars, sodium, emulsifiers, microbial transglutaminase (food additive) and nano-particles may also be triggers for excessive zonulin release.

The key is to first eliminate exposure to the trigger(s) of excessive zonulin release into the lumen. Possible interventions to restore the gastrointestinal mucosal barrier include dietary changes, treatment of dysbiosis, digestive supports and anti-inflammatory supplements; specifically quercetin, vitamin C, curcumin, gamma-linoleic acid, omega-3 fatty acids (EPA, DHA), and aloe vera. Other nutrients such as zinc, beta-carotene, pantothenic acid, and L-glutamine may provide some support for rejuvenation of the mucosal barrier. The use of some probiotics has been shown to reduce serum and fecal zonulin levels, and inulin (about 10 grams per day) lowered serum zonulin after just 5 days in healthy young subjects. Consider a Comprehensive Stool Analysis to further investigate potential causes of increased intestinal permeability.

Zonulin expression and release in the small intestine occurs when the chemokine receptor CXCR3 is stimulated by gliadin or other chemokines and induces pro-inflammatory signaling pathways in gastrointestinal epithelial cells. The released zonulin activates the cell-signaling pathway via epidermal growth factor (EGFR) and protease-activated receptor 2 (PAR2), which disassembles the tight intercellular junctions. The loss of the tight junctions increases intestinal permeability and allows polypeptides and other macromolecules to pass between epithelial cells into the lamina propria layer of the gut wall. The resultant influx of macromolecules and polypeptides induce an antigen response and promote pro-inflammatory cytokine production in the enteric immune system.

Zonulin is a pre-haptoglobulin; levels are modulated by the presence or absence of the gene haptoglobin (HP). HP-1-1 genotypes have zero (null) copies of the HP gene. HP-2-2 genotypes have two copies of the gene, and HP-1-2 genotypes have one copy of the gene. HP 1-1 (null) genotypes may have zonulin levels in the normal range, even if the presence of inflammatory or autoimmune disease is confirmed by other biomarkers. Zonulin levels may increase in nephrotic syndrome (Hp2-1 or 2-2 phenotypes).

When zonulin is cleaved by intestinal trypsin IV, it is converted into haptoglobulin, a protein with heme (iron)-binding and anti-microbial properties.

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## SPECIMEN DATA

### Comments:

Date Collected: 02/01/2018  
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Methodology: ELISA

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