

## CLINICAL SPECIFICATIONS

### OCCLUDIN / ZONULIN

#### Function:

The gastrointestinal tract is lined by a protective epithelium. The tightness and stability of this barrier is regulated by a series of intercellular junctions, collectively called tight junctions.<sup>1,3</sup> These junctions allow a regulated entry of selected molecules. The integrity of the intestinal barrier is vital for the protection of the body against antigen invasion and for the preservation of gut microchemical homeostasis.<sup>3</sup> Zonulin and occludin proteins constitute the majority of the building blocks of the tight junctions.<sup>2,6</sup>

#### Antibodies Appear:

Celiac disease<sup>2</sup>  
 Inflammatory bowel disease<sup>3</sup>  
 Type 1 diabetes<sup>5</sup>  
 Autoimmunity

**Known Cross-Reactions:** *C. jejuni* CDT, *C. jejuni*<sup>7</sup>

#### Clinical Significance:

The detection of antibodies against occludin/zonulin indicates that normal regulation of tight junctions is compromised,<sup>4,5,6</sup> and that the tight junctions are breaking<sup>1</sup> down due to an autoimmune mechanism initiated by environmental triggers such as infections, toxic chemicals, and some dietary proteins and peptides. When occludin/zonulin antibody levels are measured in conjunction with levels for lipopolysaccharide (LPS) and actomyosin, the resulting information can provide a more accurate diagnosis. The detection of positive occludin/zonulin antibody levels alone indicates a paracellular breakdown of the intestinal barrier that is triggered by factors other than bacterial antigen infiltration.<sup>4</sup> The presence of antibodies against both occludin/zonulin and LPS indicates that the integrity of the intestinal barrier has been breached by bacterial antigens through the paracellular pathway. And elevated antibody levels for occludin/zonulin, LPS, and actomyosin indicates that there has been penetration through both the transcellular and paracellular pathways. In many autoimmune diseases, including Celiac disease and Type 1 diabetes,<sup>5</sup> the onset of the disease is usually preceded by occludin/zonulin upregulation. Genetically susceptible patients who test positive for occludin/zonulin should be further assessed, monitored, and set on a preventive program for Type 1 diabetes and other autoimmune disorders.

#### References:

1. Chen, et al. COOH terminus of occludin is required for tight junction barrier function in early *Xenopus* embryos. *J Cell Biol*, 1997; 138(4):891-899.
2. Fasano. Intestinal zonulin: open sesame! *Gut*, 2001; 49:159-162.
3. Gassler, et al. Inflammatory bowel disease is associated with changes of enterocytic junctions. *Am J Physiol Gastrointest Liver Physiol*, 2001; 281:G216-G228.
4. Sander, et al. Rapid disruption of intestinal barrier function by gliadin involves altered expression of apical junctional proteins. *FEBS Let*, 2005; 579:4851-4855.
5. Sapone, et al. Zonulin upregulation is associated with increased gut permeability in subjects with Type 1 Diabetes and their relatives. *Diabetes*, 2006; 55:1443-1449.
6. Wong and Gumbiner. A synthetic peptide corresponding to the extracellular domain of occludin perturbs the tight junction permeability barrier. *J Cell Biol*, 1997; 136(2):399-409.
7. Vojdani and Vojdani. Reaction of antibodies to *Campylobacter jejuni* and cytolethal distending toxin B with tissues and food antigens. *World J Gastroenterol*, 2019; 25(9): 1050-1066.