

## **CLINICAL SPECIFICATIONS**

# **GLIADIN TOXIC PEPTIDES**

Function:	Associated With:
Gliadin Toxic Peptides (GTPs) are a group of peptides highly resistant to digestion. GTPs bind to receptors on intestinal epithelial cells.	Celiac disease <sup>1</sup> Crohn's disease <sup>1</sup> Arthritis <sup>2, 3</sup> Tubulointerstitial injury <sup>4</sup>

### **Known Cross-Reactions:**

### **Clinical Significance:**

The outcome of GTPs varies from individual to individual because different ligands for the same receptor induce very different biological effects.<sup>5,6</sup> As the name implies, GTPs are targets for tissue receptors. When gliadin binds with this specific chemokine receptor, intestinal zonulin is released.<sup>7</sup> A release of zonulin signals intestinal tight junctions to open, which puts the body at risk for autoimmunity. The ability of GTPs to restructure cytoskeletal proteins,<sup>7,8</sup> breaks the intestinal barrier allowing for the infiltration of dietary proteins, gut bacterial toxins and other environmental antigens into the submucosa and into circulation. Here, immune responses against alien antigens can lead to autoimmunities. GTPs are more abundantly expressed in the epithelium and lamina propria in patients with Celiac disease in comparison to non-celiac controls.<sup>7</sup> When GTPs bind to IgG+ plasma cell precursors, they can migrate into inflamed tissue, thereby fueling systemic inflammatory autoimmune responses.<sup>8</sup> Once B cells are activated to GTPs, memory B cells secrete antibodies to GTPs, which perpetuates systemic inflammation.<sup>7</sup> In addition to gastrointestinal disorders, GTPs have been shown to play a role in angiogenesis and cancer.<sup>9</sup>

#### **References:**

- 1. Vojdani and Vojdani. Gluten and non-gluten proteins of wheat as target antigens in autism, Crohn's and Celiac disease. J Cereal Sci, 2017; 75:252-260.
- 2. Pease and Williams. The attraction of chemokines as a target for specific anti-inflammatory therapy. Br J Pharmacol, 2006; 147(Suppl 1):S212-S221.
- 3. Boyle et al. Chemokine receptor CXCR3 agonist prevents human T-cell migration in a humanized model of arthritic inflammation. PNAS, 2012; 109(12):45998-4603.
- 4. Segerer et al. CXCR3 is involved in tubulointerstitial injury in human glomerulonephritis. Am J Pathol, 2004; 164(2):635-649.
- 5. Colvin et al. Intracellular domains of CXCR3 that mediate CXCL9, CXCL10, and CXCL11 function. J Biologic Chem, 2004; 279(29):30219-30227.
- 6. Meiser et al. The chemokine receptor CXCR3 is degraded following internalization and is replenished at the cell surface by de novo synthesis of receptor. J Immunol, 2008; 180:6713-6724.
- 7. Lammers et al. Gliadin induces an increase in intestinal permeability and zonulin release by binding to the chemokine receptor CXCR3. Gastroentrology, 2008; 135(1):194-204.
- 8. Meuhlinghaus et al. Regulation of CXCR3 and CXCR4 expression during terminal differentiation of memory B cells into plasma cells. Blood, 2005; 105:3965-3971.
- 9. Boyé et al. The role of CXCR3/LRP1 cross-talk in the invasion of primary brain tumors. Nat Commun, 2017; 8(1):1571.

www.JoinCyrex.com