DIARECT
Part of BBI Solutions

Tissue Transglutaminase and Gliadin

Celiac disease (CD) is a chronic gastrointestinal disorder most likely caused by an abnormal immune reaction to wheat gliadin and related gluten components from barley, rye, and possibly oats (Arentz-Hansen *et al.* 2000). Originally thought to be predominantly diagnosed in populations of European origin, newer studies indicate that other regions of the world have similar diagnostic rates. Worldwide, CD exerts a prevalence of approximately 1%, although the numbers can vary between different countries (Lionetti and Catassi 2011).

The disease is characterized by flattening of the jejunal mucosa and intestinal lesions of variable severity in genetically predisposed individuals. CD does not fit the typical characteristics of an autoimmune disease; yet it is associated with the occurrence of autoantibodies. Dietary gluten induces the production of antibodies against gliadin and the human endogenous tissue transglutaminase (tTG). The diagnosis of CD involves the serological analysis for the presence of anti-tTG and anti-gliadin antibodies with the analysis of the former showing both a higher sensitivity and specificity. Furthermore, the levels of these autoantibodies appear to highly correlate with the activity and severity of the disease, and are therefore especially useful for the patient's dietary and therapeutic monitoring (Schuppan *et al.* 2013).

Traditionally, tTG isolated from guinea pig tissue has been used as the antigen in the development of diagnostic tests for CD. Since guinea pig and human tTG are only 80% identical, efforts were increased to produce recombinant human tTG (Gentile *et al.* 1991; Wong *et al.* 2002).

DIARECT's recombinant human tTG antigens have been specifically modified for improved handling: substitution of an amino acid within the enzymatic active site eliminates tTG's intrinsic protein cross-linking activity while maintaining its native three-dimensional structure and secondary GTPase activity. This engineering assures reproducible properties of the recombinant antigen preparations by eliminating variable and ill-defined covalent aggregates between human tTG and host-cell proteins (Nurminskaya *et al.* 2012).

Two recombinant human tissue transglutaminase forms expressed in baculovirus/insect cells and *E. coli,* respectively, are available from DIARECT.

Monitoring of gliadin antibodies is recommended in patients, who may test negative for anti-tTG autoantibodies, in the screening of populations at risk for CD, and other

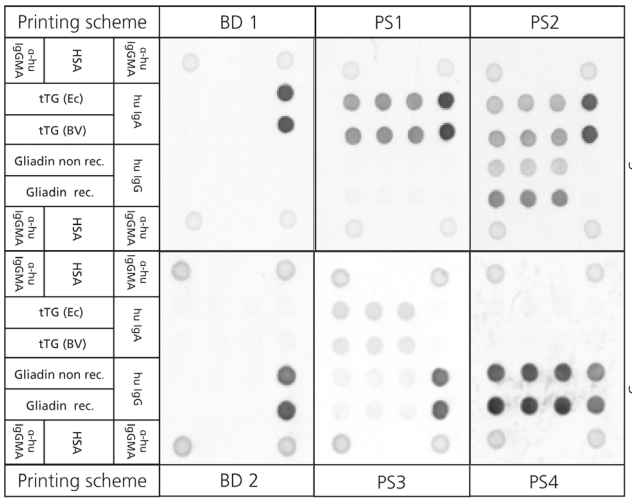

Figure: Immunodot analyses of sera from blood donors (BD1-2) and patients with celiac disease (PS1-4) for the presence of IgA (upper panel) and IgG autoantibodies (lower panel) directed against tissue transglutaminase (tTG) and/or gliadin. Antigens were spotted in triplicates on a nitrocellulose membrane as indicated. Human serum albumin (HSA) served as a negative control, anti-human IgGMA (α-hu IgGMA) and human IgG (hu IgG) were used as positive controls.

gluten-sensitive enteropathies (Schuppan *et al.* 2013).

DIARECT has successfully completed the recombinant protein approach by designing and producing a deamidated γ-gliadin isoform. Based on the sequence design, the epitopes present in this recombinant gliadin correspond to the deamidated neo-epitopes, which are formed in the natural gliadin antigen by transglutaminase-mediated glutamine side chain deamidation (Schwertz *et al.* 2004).

DIARECT's recombinant gliadin is produced in *E. coli* and non recombinant gliadin is isolated from wheat (*Triticum aestivum)* grain.

Ordering Information		
15200	Tissue Transglutaminase	0.1 mg
15201	(tTG; expressed in Baculovirus/Sf9)	1.0 mg
14400	Tissue Transglutaminase	0.1 mg
14401	(tTG; expressed in *E. coli*)	1.0 mg
19500	Gliadin (recombinant; deamidated)	0.1 mg
19501		1.0 mg
31500	Gliadin (non recombinant)	0.1 mg
31501		1.0 mg

References:
Arentz-Hansen *et al.* (2000) Gut. 46 (1): 46-51
Gentile *et al.* (1991) J Biol Chem. 266 (1): 478-483
Leonard *et al.* (2014) Clin Exp Gastroenterol. 24: 25-37
Lionetti and Catassi (2011) Int Rev Immunol. 30 (4): 219-231
Nurminskaya *et al.* (2012) Int Rev Cell Mol Biol. 294: 1-97
Schuppan *et al.* (2013) Dtsch Arztebl Int. 110 (49): 835-846
Schwertz *et al.* (2004) Clin Chem. 50 (12): 2370-2375
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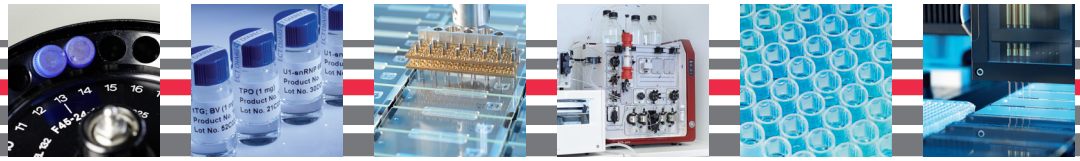

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