Approaches to Establish Thresholds for Major Food Allergens and for Gluten in Food. III, IV, V.

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III. Celiac Disease

A. Introduction

Celiac disease (also known as celiac sprue and gluten sensitive enteropathy) is a chronic inflammatory disorder characterized by mucosal damage to the small intestine leading to gastrointestinal illness, nutrient malabsorption, and a wide range of clinical manifestations (NIH, 2004; Shan, *et al.* 2002). There is a consensus opinion that celiac disease is caused by an aberrant (T lymphocyte) immune response to dietary glutens predominantly found in wheat, barley, and rye (NIH, 2004). However, there is evidence that at least some persons who have celiac disease may not tolerate oats (Lundin *et al*., 2003; Arentz-Hansen *et al*., 2004). Those individuals who have a genetic predisposition to celiac disease react to peptides within the proline- and glutamine-rich protein fractions of the grains (Dewar *et al*., 2004). For affected individuals, celiac disease is a lifelong condition and, if not treated, is associated with significant morbidity and increased mortality (Fasano, 2003; Corrao *et al*., 2001; Dewar *et al*., 2004). There is no cure for celiac disease (NIH, 2004). Strict avoidance of potentially harmful concentrations of glutens in the diet is the only known means of completely preventing the clinical and pathological complications of celiac disease (NIH, 2004; Fasano and Catassi, 2001).

B. Mechanism of Pathogenesis

Celiac disease is characterized by injury to the mucosa of the small intestine and specifically targets the fingerlike projections, called villi, where absorption of key nutrients takes place (Figure III-1). This injury is believed to be due to an autoimmune disorder involving modification of the antigenic presentation of gluten in the intestinal tract of genetically predisposed individuals expressing the major histocompatibility haplotypes HLA-DQ2 or HLA-DQ8 (Farrell and Kelly, 2002; Fasano, 2003). In these individuals, binding of the enzyme tissue transglutaminase (tTG) to wheat gluten (a glutamine rich protein) potentiates uptake and presentation by antigen-presenting cells in the lamina propria, triggering a vigorous T-cell response (Schuppan and Hahn, 2002), leading to production of IgG and IgA antibodies directed to wheat gluten peptides (i.e., gliadins and glutenins) and to tissue