Title: Celiac Disease *GeneReview* – Therapies Under Investigation
Authors: Taylor AK, Lebwohl B, Snyder CA, Green PHR
Updated: September 2015
Note: The following information is provided by the authors and has not been reviewed by *GeneReviews* staff.

Therapies Under Investigation

Lifelong adherence to a gluten free diet is currently the only treatment for celiac disease. However, many novel therapeutic approaches are being investigated that potentially could be used as alternatives for or additives to a gluten-free diet, as reviewed by Castillo et al [2015] and Rashtak & Murray [2012]. Investigation of therapeutic approaches is limited by lack of an animal model for celiac disease.

- Inhibitors of the zonulin pathway that act to prevent gliadin from inducing increased intestinal permeability. Larazotide (AT-1001) is a tight junction regulatory peptide and zonulin antagonist. Taken orally that acts as an intestinal permeability blocker. This drug is in clinical trials.

- Peptides that block the binding groove of DQ2 and DQ8 to prevent activation of gluten-sensitive T cells. The viability of this approach is currently uncertain.

- Transglutaminase (tTG) inhibitors are being investigated.

- Cytokine blockers, particularly for refractory celiac disease

- Drugs that selectively inhibit leukocyte adhesion and migration of lymphocytes into inflamed tissues

- Detoxifying gluten, eg. by oral proteases. Three candidate drugs are in clinical trials. The gluten dose that can be detoxified by specific enzyme doses is not yet known.

- Gluten-sequestering polymers. An oral polymeric resin, P(HEMA-co-SS) binds to gluten and is under study.

- Gluten tolerization. A peptide-based vaccine that could desensitize or induce tolerance in individuals with celiac disease. A prototype vaccine, Nexvax2, involves a set of gluten peptides recognized by HLA-DQ2 is in clinical trials.

Other potential therapeutic targets

As reviewed in Sollid & Khosla [2011], other potential therapeutic targets involve pathways in common with other disorders. These include Rho/Rho kinase inhibition to theoretically reverse gluten-dependent increase in intestinal permeability and antibodies to proteins involved in autoimmune pathologies, including anti-IFN-γ, anti-CD3, anti-CD20 therapy, and anti-IL-15. Interfering with the homing of gluten-specific T cells to the gut musoca by using CCR9 antagonists is another approach, and a phase II clinical trial is listed in Sollid & Khosla [2011].

References

Castillo NE, Theethira TG, Leffler DA. The present and the future in the diagnosis and management of celiac disease. Gastroenterol Rep (Oxf). 2015;3:3-11.

Rashtak S, Murray JA. Review article: Coeliac disease, new approaches to therapy. Aliment Pharmacol Ther. 2012;35:768-81.

Sollid LM, Khosla C. Novel therapies for coeliac disease. J Int Med. 2011;269:604-13.