

Gut Reaction

How celiac disease is triggered and might be treated



Villi

Finger-like projections that line the small intestine



Enterocytes

Cells on the surface of the villi



In someone with celiac disease, undigested gluten fragments trigger a reaction by the immune system in the small intestine.



The reaction occurs in a series of steps, which ultimately damage the villi and prevent nutrients from being absorbed.



Potential new celiac disease treatments would interfere with the reaction at different points in the process.



These are undigested gluten fragments in the small intestine.



Some gluten fragments pass through the enterocytes, those cells lining the surface of the small intestine.



These gluten fragments can now build up under the enterocytes.



This "build up" causes the enterocytes to send a chemical signal to the immune system that something is wrong.



The signal is received by the immune system cells...



...which then attack and damage the enterocytes.



This damage causes loosening of the tight junctions between the enterocytes. Normally, nothing can pass between these cells...



...but now that there is space between the enterocytes, more undigested gluten fragments pass through.



Also, the partially-damaged enterocytes release an enzyme, called tTG.



Next, the tTG attaches to the gluten fragments.



When tTG attaches to gluten, it changes the gluten in a way that sets off the primary immune system response.



The gluten that has been changed is picked up by special white blood cells, called antigen-presenting immune cells.



These white blood cells present the gluten using a receptor on the surface of the white blood cells.



By presenting the gluten, the receptor signals to another type of immune system cell, called a Helper T-Cell.



T-Cells fight disease in the body, but in celiac disease T-Cells are triggered by gluten to mistakenly attack the enterocytes.



The Helper T-Cells secrete chemicals that cause three things to happen...



First, the Helper T-Cells release toxic secretions...



...that directly damage the enterocytes.



Second, the Helper T-Cells signal the Killer T-Cells.



The Killer T-Cells begin to fight...



...and directly attack the enterocytes.



Third, the Helper T-Cells signal to Mature B-Cells.



These mature B-Cells then make two types of antibodies:



One type of antibody attaches to gluten fragments, and the other attaches to the tTG enzyme.



This antibody activity is very close to the enterocytes and may also cause additional damage to these cells.



Also, scientists theorize that in response to gluten, *zonulin*, a molecule made by the body and linked to inflammation, ...



...may play a role in loosening the tight junctions earlier in the process.



Potential treatments for celiac disease are designed to interrupt different steps in the disease process.



Target: Undigested gluten fragments

A drug in this category would bind to gluten in the small intestine, so gluten would never get absorbed by the body in the first place.



Binding gluten so it's not absorbed

Target: Undigested gluten fragments

A drug in this category would use enzymes to break down gluten into smaller particles.

The particles would then be too small to stimulate an immune response.

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Breaking down gluten using enzymes

Target: The tTG Enzyme

A drug in this category would prevent tTG from modifying gluten.

If tTG does not change the gluten, this would help to reduce an abnormal immune response.



Preventing the enzyme tTG from modifying gluten in the cell, which helps to reduce an abnormal immune response

Target: Cells that react to gluten

A drug in this category would target the cells that react to gluten.

With no immune reaction, the T-Cells would not get activated.



Inducing immune tolerance to protect against the effects of gluten by preventing an immune reaction

Target: Immune reactions

A drug in this category would interrupt the immune reactions that do occur.

If the reaction gets interrupted, the immune system would not attack the enterocytes.



Interrupting the immune reactions that occur

Target: Gaps between enterocytes

A drug in this category would prevent the opening of gaps between the enterocytes.

Without gaps between these cells, the gluten would not pass through to trigger the immune system.



Interrupting the immediate or delayed effects of gluten on the cells lining the intestine

Researchers are investigating these ways of treating celiac disease, which could lead to a drug or vaccine that would prevent symptoms and intestinal damage and eventually lead to a cure.

Go Beyond Celiac is designed to help advance this research by collecting and compiling important patient stories and data.



Visit www.Go.BeyondCeliac.org

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