

# Researchers find increased zonulin levels among celiac disease patients

**Public release date: 28-Apr-2000**

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Researchers at the University of Maryland School of Medicine have found that the human protein zonulin, which regulates the permeability of the intestine, is at increased levels during the acute phase of celiac disease. The discovery suggests that increased levels of zonulin are a contributing factor to the development of celiac disease and other autoimmune disorders such as insulin dependent diabetes, multiple sclerosis, and rheumatoid arthritis. The findings are published in the April 29 issue of the journal Lancet.

"Zonulin works like the traffic conductor or the gatekeeper of our body's tissues," says lead author Alessio Fasano, M.D., professor of pediatrics and physiology at the University of Maryland School of Medicine, and director of Pediatric Gastroenterology and Nutrition at the University of Maryland Hospital for Children. "Our largest gateway is the intestine with its billions of cells. Zonulin opens the spaces between cells allowing some substances to pass through while keeping harmful bacteria and toxins out," explains Dr. Fasano.

Earlier research conducted by Dr. Fasano discovered that zonulin is also involved in the regulation of the impenetrable barrier between the blood stream and the brain, known as the blood-brain barrier. Celiac disease offered Dr. Fasano and his team a unique model for understanding the dynamic interaction between zonulin and the immune system. Celiac disease is a genetic disorder that affects one out of every 300 people in Europe, but its prevalence in the United States is not fully known. People who suffer from the disorder are unable to eat foods that contain the protein gluten, which is found in wheat and other grains. The gluten sets off a reaction that can cause diarrhea, abdominal pain, malabsorption of nutrients, and other gastrointestinal problems. Celiac disease can be easily treated by avoiding foods with gluten.

With celiac disease, the body reacts to gluten by creating antibodies that attack the intestine and cause severe damage over time. Unlike other autoimmune disorders, scientists also know that celiac disease is triggered by a specific antigen, which is the protein gluten. Celiac disease is also known to cause increased permeability of the intestine. In addition, many

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people who suffer from celiac disease also suffer from other autoimmune disorders.

The research team examined the intestinal tissue of seven people with celiac disease, and six patients without the disease. Patients with active celiac disease showed higher levels of zonulin and anti-zonulin antibodies compared to non-celiac patients and patients in remission, who were eating a gluten-free diet.

"With celiac disease, we could never understand how a big protein like gluten was getting through to the immune system. Now we have the answer," explains Dr. Fasano. "People with celiac have an increased level of zonulin, which opens the junctions between the cells. In essence, the gateways are stuck open, allowing gluten and other allergens to pass. Once these allergens get into the immune system, they are attacked by the antibodies," adds Dr. Fasano.

"I believe that zonulin plays a critical role in the modulation of our immune system. For some reason, the zonulin levels go out of whack, and that leads to autoimmune disease," explains Fasano.

Dr. Fasano adds that more research is needed. He is currently conducting experiments with diabetic rats. Preliminary results from his experiments show that insulin dependent diabetes occurs in lab rats about three to four weeks after increased intestinal permeability. The researchers believe the increased intestinal permeability is associated with increased levels of zonulin.

"We are at the threshold of exciting discoveries in this field," says Dr. Fasano. "We now have a new way of looking at our cells. Our cells are not stacked together like bricks. They are a dynamic field, which is constantly in flux." ###