

Fluorescent image of a skin sample, where the nuclei are blue, transglutaminase 3 is green, and IgA antibodies (immunoglobulins) are red. Yellow areas indicate overlapping location of IgA and transglutaminase 3 in the skin.

Kaunisto studies immune cells and the immune response to find out why some people with celiac disease develop dermatitis herpetiformis.

“It should be remembered that the gut and the skin have different layers that function in different immunological ways. Dermatitis herpetiformis is a really good target for studying the extra-intestinal symptoms of celiac disease. This information can then also be used to investigate other autoimmune diseases. For example, how can rheumatism start in one place and then spread elsewhere and become systemic?”

Around 10 per cent of people with celiac disease have dermatitis herpetiformis. Celiac disease and dermatitis herpetiformis can be investigated by measuring antibodies in the blood. In people with celiac disease and those with dermatitis herpetiformis, gluten triggers the formation of tissue antibodies.

“Celiac disease is known as an intestinal disease, but it has many other symptoms that are not related to the intestines at all. There may be neurological and skin problems too. Is there a difference in immunity between people with celiac disease and people with dermatitis herpetiformis? How can an immune response spread from the gut to the skin – and why does a rash develop?”

The diagnosis of celiac disease exploits the analysis of antibody levels. Transglutaminases are enzymes that bind proteins together in tissues. High levels of antibodies to transglutaminase 2 (S-tGAbA) suggest the person has celiac disease. Transglutaminase 2 modifies the structure of gluten in the body. This causes the lining of the small intestine to become inflamed and damaged.

The Celiac Disease Research Center in Tampere has conducted a study in which patients with dermatitis herpetiformis who were on a gluten-free diet were exposed to gluten for a short period. Before and during exposure, samples were taken from the

small intestine and blood. These samples are studied to find out how gluten affects the expression of RNA in blood cells and the small intestine.

“Although some people with celiac disease have the same serum-based antibodies as people with dermatitis herpetiformis, not everyone will get dermatitis herpetiformis”, says Kaunisto.

“Patients with dermatitis herpetiformis have antibodies to transglutaminase 2, but they also have antibodies to a related enzyme, transglutaminase 3. Transglutaminase 3 (TG3) antibodies are also found in the skin, close to the rash, and are thought



CSC can install new software on CSC’s computing environment SD Desktop at the researcher’s request.

to be involved in its development. TG3 antibodies are also found in the bloodstream of patients with dermatitis herpetiformis. Although some people with celiac disease also have antibodies to transglutaminase 3 in the bloodstream, not all people with celiac disease develop dermatitis herpetiformis. Why this is so is what we want to solve.”

According to Kaunisto, the research is of great benefit to clinical science.

“For example, if celiac disease is not well managed – the person doesn’t stick to a strict gluten-free diet, say – is there a greater chance of developing extra-intestinal symptoms?”

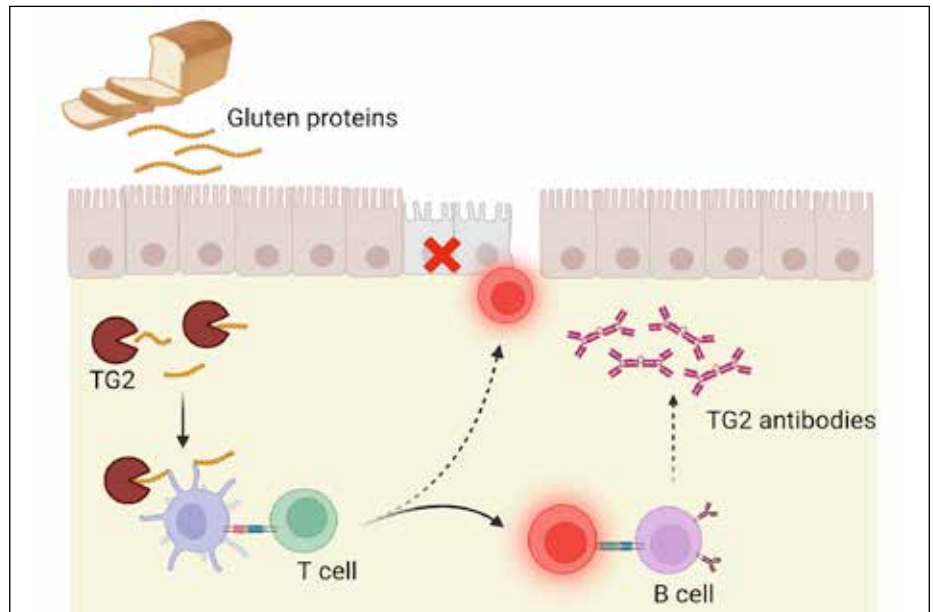
### CSC’s sensitive data services

The study involves analysis of sensitive data obtained from patient’s tissue samples. Patients consented to participate in the study. As this is information subject to the European Union’s General Data Protection Regulation (GDPR), the data will be processed and used in CSC’s sensitive data services (SD Desktop and SD Connect).

The sequencing has been done in collaboration with the University of Helsinki, and the data is stored encrypted in SD Connect and analysed with SD Desktop.

Kaunisto did not have previous experience of the high-performance computing or sensitive data services.

“I started using the Sensitive Data Services because I needed more computational power than what was available for me through the university, and I needed a secure environment for this computational power. I find the services very easy to use as the online guides are very thorough. If I have a



*The inflammatory reaction in the small intestine. Transglutaminase 2 (TG2) modifies gluten proteins, which are presented to the T-cells. T-cells cause inflammation that leads to the dysregulation and apoptosis of the epithelial cells. T-cells also activate antibody-producing B-cells to produce the antibodies targeting to TG2. In the picture the red X indicates changes in the gut that leads to the damage or destruction of intestinal cells.*

problem I can’t solve myself the helpdesk is always very helpful.”

To avoid the long-term effects of gluten, treatment can begin as soon as possible when celiac disease is detected early. However, since gluten is present in many foods, gluten-free diets are difficult to maintain.

“At the moment, the only treatment is a strict gluten-free diet, but there is also a lot of research underway into pharmaceuticals as possible future treatments. The Celiac Disease Research Center also collaborates

extensively with companies developing new potential drugs. Drugs may be able to prevent intestinal and other damage in patients in the future, but initially they will likely be adjunctive therapies alongside gluten-free dietary treatment. A preliminary study carried out in Tampere University found that the experimental-phase drug ZED1227 inhibited transglutaminase 2 activity, and its use reduced gluten-induced intestinal damage in patients.”

12.4.2023 | Ari Turunen

### MORE INFORMATION:

**Celiac Disease Research Center, University of Tampere**  
<https://www.tuni.fi/en/research/ce-lic-disease-research-center>

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