

Gluten contributes to the development of rare, deadly blood cancer in a small group of coeliac patients

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Dr Jeroen van Bergen pointing at CyTOF2 mass spec machine. Credit: Worldwide Cancer Research

Scientists in The Netherlands have revealed how gluten plays a role in

the development of a rare form of cancer, for some people with coeliac disease.

The scientists at Leiden University Medical Center (LUMC) have shown that [immune system cells](#), which react to gluten, produce chemicals called cytokines that can contribute to the development of a rare form of lymphoma ([cancer](#) of the white blood [cells](#)).

The findings were published in the *Proceedings of the National Academy of Sciences (PNAS)*. LUMC researcher and Worldwide Cancer Research scientist, Dr Jeroen van Bergen, explained: "the immune system is seen as an ally in the battle against cancer, but that isn't always the case."

Refractory coeliac disease

Coeliac disease is an autoimmune disease where special immune system cells, called gluten-specific T cells, have an extraordinarily strong inflammatory reaction to gluten. The cells produce chemicals, called cytokines, which then stimulate other immune system cells.

Coeliac patients control their symptoms by following a gluten-free diet. However, a small percentage (2-5%) of patients diagnosed in adulthood does not respond to such a diet, due to long term inflammation and damage, and have what is called refractory coeliac disease (RCD).

In one type of refractory coeliac disease, called RCDII, immature [white blood cells](#) from the [immune system](#) (called lymphocytes) which are located in the wall of the small intestine, multiply in number in an uncontrolled manner. In about half of the patients, these cells develop into a malignant, incurable form of white blood cell cancer called enteropathy-associated T-cell lymphoma (EATL), an exceptionally rare and aggressive type of lymphoma arising from the inflammation caused by the body's reaction to gluten.

Growth factors

Scientists know that the [lymphoma cells](#) are dependent on a cytokine called IL-15 which encourages cells to multiply. Here the researchers have shown that cell proliferation can be stimulated just as effectively by three other cytokines, TNF, IL-2 and IL-21. These three cytokines are produced by the gluten-specific T cells, in response to gluten. The new findings thus provide a potential mechanism by which the immune response to gluten contributes to the growth of malignant cells in RCDII and opens up new avenues of research.

Targeted treatments

An important question now is to find out at which stage of lymphoma development these cytokines are involved.

Dr van Bergen explained: "It is likely that at the time of lymphoma diagnosis, the patient has already experienced decades of intestinal inflammation. We need to determine the extent to which it would actually help to block these newly discovered growth factors with targeted drugs at the time of diagnosis. In the meantime, we have tested a large number of potential drugs in the laboratory, and two of them seem promising. But as I said, this is only interesting in terms of a new treatment if these [growth factors](#) still have a role to play in the growth and development of the [lymphoma](#) after diagnosis."

Dr Lara Bennett, Science Communications Manager at Worldwide Cancer Research added "This is another great example of the importance of early-stage, discovery research. This is a rare type of cancer but the findings could be of real benefit to this small but important group of patients with refractory coeliac [disease](#)."

More information: Yvonne M. C. Kooy-Winkelaar et al. CD4 T-cell cytokines synergize to induce proliferation of malignant and nonmalignant innate intraepithelial lymphocytes, *Proceedings of the National Academy of Sciences* (2017). [DOI: 10.1073/pnas.1620036114](https://doi.org/10.1073/pnas.1620036114)

Provided by Leiden University Medical Center

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