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# Aberrant epigenetic regulation behind the intestinal symptoms in coeliac disease

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Researchers at the University of Tampere discovered a mechanism causing aberrancies in coeliac disease and colorectal cancer.

Researchers at the University of Tampere discovered a regulation mechanism governing the intestinal homeostasis. Disturbances in this mechanism are implicated in coeliac disease and possibly also in colorectal cancer. The study provides new information on the pathogenesis of the differentiation defect of the epithelium in the small intestine in coeliac disease.

Coeliac disease is an autoimmune disease in genetically susceptible individuals and is triggered by gluten, a protein found in wheat and other grains. In coeliac disease, ingested dietary gluten causes intestinal mucosal damage with villus atrophy and crypt hyperplasia. At the cellular level, epithelial cells are less differentiated and hyper-proliferative leading to the malabsorption of nutrients.

Researchers discovered that a certain epigenetic mechanism (Polycomb) governs the homeostasis between the intestinal stem cells in the crypt and the differentiated epithelium in the villi. Polycomb is silencing the genes epigenetically by methylating histone proteins that are packing the DNA.

"Polycomb is well-known for its function to regulate embryonal development. We discovered that Polycomb is also able to regulate the homeostasis of the small intestine in adults. The regulation of intestinal

homeostasis is a tremendous task as the epithelium of the intestine needs to be replenished completely every 4-5 days," says Academy of Finland Postdoctoral Researcher and Principal Investigator Keijo Viiri.

This work, funded by the Academy of Finland, shows that in coeliac disease, dietary gluten induces excessive activity of Polycomb leading to the aberrant silencing of genes necessary for the differentiation of villus epithelium and to the concomitant differentiation defect in coeliac disease. In addition, the study shows that Polycomb target genes are dysregulated also in colorectal cancer, suggesting that aberrant Polycomb activity is a common attribute in intestinal diseases entailing a differentiation defect on the intestinal epithelium.

This work was conducted in the Tampere Center for Child Health Research at the University of Tampere and was published in the journal *Stem Cells*.

From a clinical point of view, this work sheds light on the pathogenesis of the intestinal damage in coeliac disease and provides diagnostic markers for the disease. As Polycomb regulates only genes imperative for development, this work is also instrumental to further understand the biology of the intestinal homeostasis. The study was performed by PhD Keijo Viiri's research group at the University of Tampere.

**More information:** Mikko Oittinen et al, PRC2 Enacts Wnt Signaling in Intestinal Homeostasis and Contributes to the Instigation of Stemness in Diseases Entailing Epithelial Hyperplasia or Neoplasia, *STEM CELLS* (2016). DOI: 10.1002/stem.2479

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