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COELIAC DISEASE

Lnc13 and coeliac disease: a link to pathogenesis?

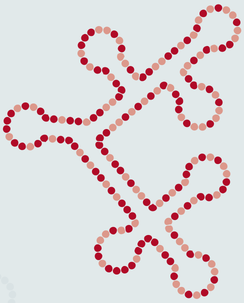
Researchers have identified and characterized a long non-coding RNA (lncRNA), lnc13, that is associated with coeliac disease. "The level of this lncRNA is dramatically reduced in the intestinal epithelium of patients with coeliac disease," notes author Sankar Ghosh.

Genome-wide association studies indicate that an important number of disease-associated single nucleotide polymorphisms (SNPs) map to non-coding and intergenic regions. Furthermore, lncRNAs represent a notable portion of genomic non-coding regions and have been identified as having a role in biological processes and disease pathogenesis. As such, Ghosh and colleagues explored how SNPs in non-coding regions and lncRNAs might be involved in disease pathology.

Disease-associated SNPs in intergenic regions were examined and, after comparisons with lncRNAs mapped in the mouse genome, a novel human lncRNA (lnc13) was found. Expression of lnc13 was confirmed in different human tissues, including the lamina propria and villi of the small intestine. Comparisons between small intestinal biopsy samples from patients with coeliac disease and those from healthy individuals revealed markedly lower levels of lnc13 in coeliac disease samples.

Next, the regulation, function and mechanisms of action of lnc13 were characterized. Lnc13 repressed pro-inflammatory gene expression under homeostatic conditions via binding to a heterogeneous nuclear ribonucleoprotein and interactions with chromatin. Notably, lnc13 regulated expression of a subset of inflammatory genes that have been related to coeliac disease, namely *TRAF2*, *STAT1*, *IL1RA* and *MYD88*. When lnc13 levels are reduced, increased expression of the repressed pro-inflammatory genes occurs, which supports downregulation of lnc13 as a factor in inflammation in coeliac disease. "Moreover, this lncRNA harbours SNPs that have been previously shown to associate with coeliac disease, and provide a mechanism by which the risk allele affects the function of the lncRNA," adds Ghosh.

> "...markedly lower levels of lnc13 in coeliac disease samples"



Laura Marshall/NPG

Alongside further work on the regulation of lnc13, the researchers hope to use a similar strategy to identify and characterize additional lncRNAs that might be implicated in other complex diseases.

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ORIGINAL ARTICLE Castellanos-Rubio, A. *et al.* A long noncoding RNA associated with susceptibility to celiac disease. *Science* **352**, 91–95 (2016)