Title: Gluten-Induced Transcriptomic Changes in Celiac Patient-Derived iPSC Small Intestinal Epithelial Cells

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Abstract
Celiac disease is an autoimmune disease that mainly affects the small intestine. In genetically predisposed individuals, gluten consumption triggers an immune reaction against the intestinal epithelium, leading to shortening of the villi and elongation of the crypts, which reduces nutrient absorption.

The aim of this work is to better understand what gene expression changes in small intestinal epithelial cells (SIECs) are induced by gliadin in celiac and healthy individuals, in the absence of other stimulants.

To study gene expression changes, we analyzed RNA-sequencing data from two induced pluripotent stem cells (iPSC) -derived SIEC lines, one from a healthy control and one from a celiac patient. The cells were stimulated for 24 hours with three different gliadins, two CRISPR-edited less immunogenic gliadins, and zein, a storage protein in maize, as control. The raw RNA-sequencing data was pre-processed, and differential gene expression analysis of protein-coding genes was performed using DESeq2. Expression levels of cell type marker genes were visualized using heatmaps.

The results show no major gene expression differences between the gliadins and zein, in celiac or healthy cell lines. Expression of intestinal epithelial cell type marker genes show that the cells have been differentiated toward small intestinal epithelium.

In conclusion, gliadin alone does not induce major transcriptomic changes in iPSC-derived SIECs. This preclinical model has a similar gene expression profile as other static iPSC-SIEC cultures.