Kukkoaho Pauliina[1], Annala Maria[1], Tanner Karoliina[1], Siddique Fatima[1], Kandikanti Niyati[1], Kaunisto Helka[1], Kesseli Juha[1], Leskinen Katarzyna[2], Saavalainen Päivi[2], Nykter Matti[1], Aalto-Setälä Katriina[1,3], Kaukinen Katri[1,3], Lindfors Katri[1], Juuti-Uusitalo Kati[1]

1) Tampere University
2) Folkhälsan and University of Helsinki
3) Heart Center, Tampere University Hospital
4) Tampere University Hospital

Celiac and non-celiac iPSC-derived small intestinal epithelial cells evince cell-type specific response to inflammatory cytokine stimulations

The apical surface of the small intestinal epithelium the location which is thought to be the first site of action in celiac disease pathogenesis. Currently there are no *in vitro* small intestinal epithelia cell (SIEC) models derived from celiac disease (CD) -patient cells that is easily accessible from both apical and basal sides, has small intestinal epithelial morphology and functions and has CD genotype

Thus, we aimed to set-up and validate two-dimensional (2D) CD-patient iPSC-SIEC *in vitro* model, that enables stimulation and assessment from both sides of the epithelial layer.

CD and healthy control (HC) iPSCs were sequentially differentiated towards SIEC. The functionality of the model was assessed under cytokine stimuli, with interferon γ and tumor necrosis factor α. The RNA sequencing, qRT-PCR, toxicity assay, and confocal microscopy were used to assess maturity and cell response to cytokines.

The confocal imaging and RNA sequencing analyses showed that the 2D-differentiaton method supports maturation of polarized enterocytes. Cytokine stimuli increased the expression of several cytokine stimulation associated genes, such as CXCL-9 or CXCL-10.

Results suggest that all iPSC lines used in here can be differentiated in 2D to SIECs, and when stimulated with cytokines relevant for celiac disease, they respond in a tissue specific manner. Data implies that our 2D-CD-iPSC-SIEC model represents an appropriate platform to study effects of CD specific stimuli in intestinal epithelium.