The small intestine is known not only for its role as a digestive organ, but also as a favorite organ for inflammatory bowel diseases (IBD). Caco-2 and Caco-animals are used as alternative models, but the problem is poor reproducibility to the human biological small intestine due to different gene expression levels and species differences. Therefore, we developed human iPSC-derived intestinal epithelial cells (F-hiSIEC) and we attempted to construct an in vitro cell assay model with properties similar to those of the human small intestine.

F-hiSIEC shows the physiological characteristics similar to those of the human small intestine. Interestingly, F-hiSIEC contains goblet cells, enteroendocrine cells, M cells, etc., which are known to exist in the intestinal epithelium. Therefore, we evaluated the function of M cells present in F-hiSIEC. As a result, particle migration from the luminal side to the vascular side was observed. We also evaluated the development of an IBD model using Caco-2 cells. When inflammatory cytokines were added to the model, TEER and the MUC2 expression was decreased, and the expression of various inflammatory cytokines was increased. When intestinal bacterial metabolites were added to the model in combination with the cytokines, both TEER and MUC2 expression were restored. In conclusion, these cells have properties similar to the human small intestine, and they are expected to be a useful tool for M-cell-mediated absorption of nanoparticles and microplastics, and as an in vitro model of IBD and leaky gut in the human small intestine.

**F-hiSIEC showed CYP3A4 activity comparable to that of human primary enterocytes.**

**CYP3A4 activities and P-gp activities of F-hiSIEC showed good reproducibility.**

**Inflammatory Bowel Disease model**

- Inflammatory bowel disease is the collective term for Crohn’s disease and ulcerative colitis, and the number of patients is increasing yearly. IBD is a multifactorial disease associated with genetic and environmental factors.
- We attempted to construct an inflammatory bowel disease model using these cells.

**Influence of Inflammatory Cytokines and SCFAs on IBD model**

- The decrease of barrier function and expression of the TJP2/CD1 and MUC2 genes with Th1f and IFNγ treatment were partially recovered by combination treatment of SCFAs.
- The F-hiSIEC-based evaluation system allowed us to reproduce the effects of SCFAs on barrier function as in the human small intestine.