DefiniGEN
DISEASE MODEL INNOVATION

Technical Data Sheet

DefiniGEN human iPSC-derived intestinal organoids

Description

DefiniGEN intestinal organoids provide a unique *in vitro* system to model the human intestine. The organoids harbor a combination of cell types normally present in the primary intestinal epithelial *in vivo*, including goblet cells, Paneth cells, enterocytes, and enteroendocrine cells. Multiple CYP450s and transporters such as SLCO2B1 and ABCB1 are also expressed in the cells. The cells can be used for drug absorption, metabolism, and transporter studies, as well as the modelling of infectious disease.

Immunocytochemistry analysis

Immunocytochemistry analysis has demonstrated that the Def-INTESTINAL organoids display a polarized epithelium and are composed of differentiated cell types with distinct morphologies. The organoids contain absorptive enterocytes as well as the major secretory lineage cell types including Paneth cells, goblet cells, and enteroendocrine cells.

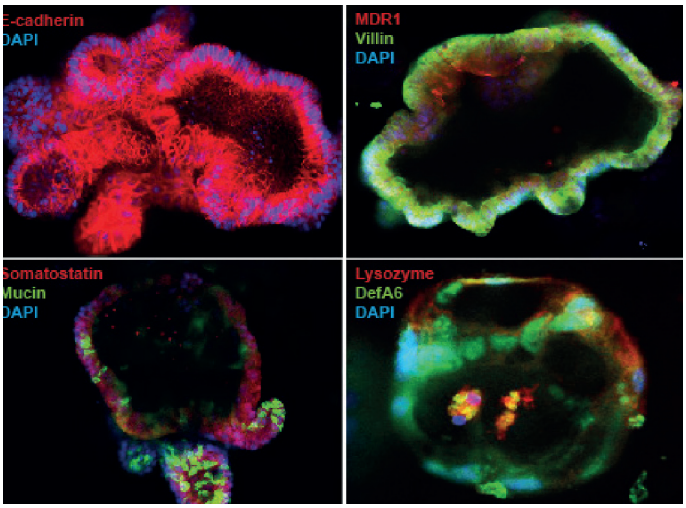

Figure 1. Organoids display specific marker gene expression profiles. Organoids display positive staining of key intestinal cell markers including; epithelial cells (E-cadherin), enterocytes (villin), goblet cells (mucin), enteroendocrine (somatostatin), and Paneth cells (lysozyme).

Advantages

Normal human genetics wild-type donor genetics and karyotype verified

Display multiple key gut markers OLFM4, CHGA, MUC2, Villin and KRT19

Cells can be used for safety drug absorption, metabolism and induction of transporters and infectious disease modelling

Organoid format provides a unique in vitro system to model human intestinal cells containing populations of goblet cells, enterocytes, Paneth cells and enteroendocrine cells

Standardized cell product containing human intestinal organoids producing reproducible and biologically relevant data

Specification

- Catalog Number Def-INTESTINAL WT
- Format Cryopreserved organoids
- Viability >70%

Cell morphology

Typical intestinal organoid morphology is observed in Def-INTESTINAL cells. The organoids initially form spheroid structures which over successive passages develop the crypt architecture characteristic of primary human intestinal organoids.

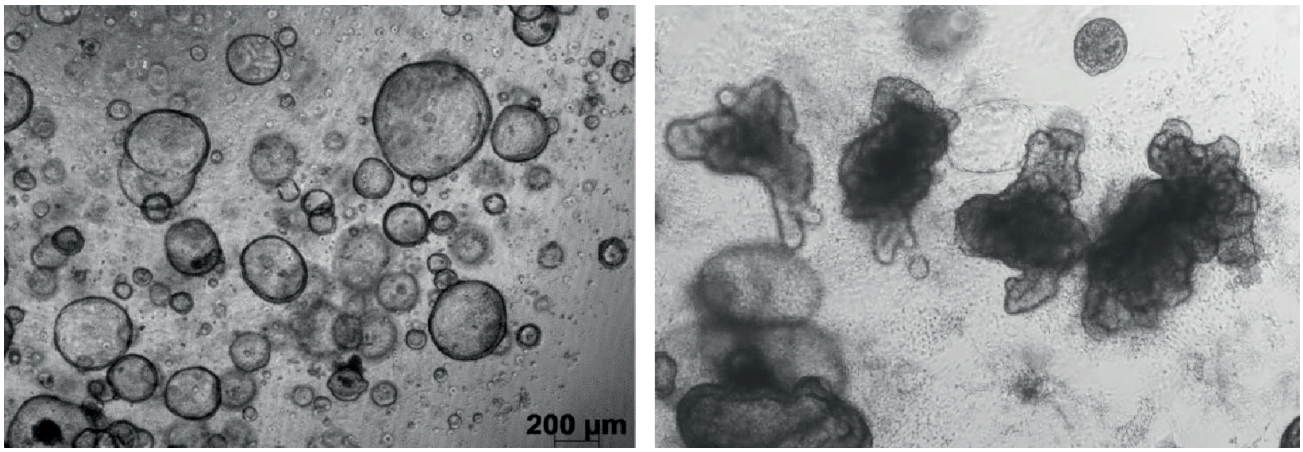

Figure 2. Typical intestinal morphology is observed in Def-INTESTINAL cells. Organoids grown encapsulated in matrigel in a 24-well plate.

Key intestinal cell marker analysis

Figure 3. Def-INTESTINAL organoids have been demonstrated to display multiple key gut markers. Gene expression analysis shows the intestinal markers KRT19, Villin, and CHGA have similar expression profiles in Def-INTESTINAL and the primary control relative to GAPDH.

Drug transporter analysis

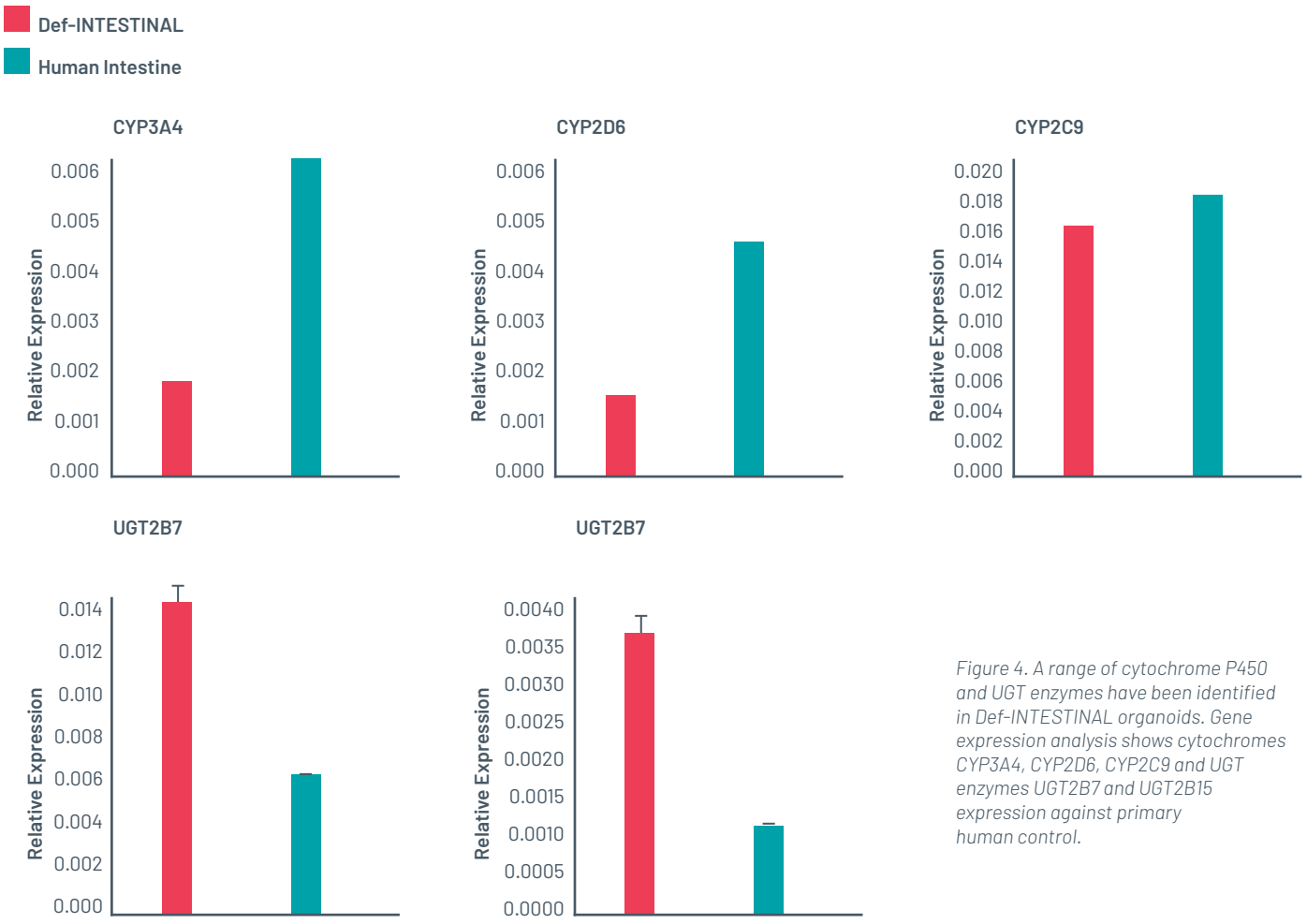

Figure 4. A range of cytochrome P450 and UGT enzymes have been identified in Def-INTESTINAL organoids. Gene expression analysis shows cytochromes CYP3A4, CYP2D6, CYP2C9 and UGT enzymes UGT2B7 and UGT2B15 expression against primary human control.

Down-regulation or inhibition of ABC efflux transporters in the intestine can be used as a strategy to improve oral drug bioavailability of known substrates as these transporters prevent drug molecules from being absorbed. Def-INTESTINAL organoids have the transporter functionality required for these studies.

The SLC (solute carrier) family have an important role in physiological processes ranging from the cellular uptake of nutrients to the absorption of drugs and other xenobiotics. SLCs are primarily involved in the uptake of small molecules into cells.

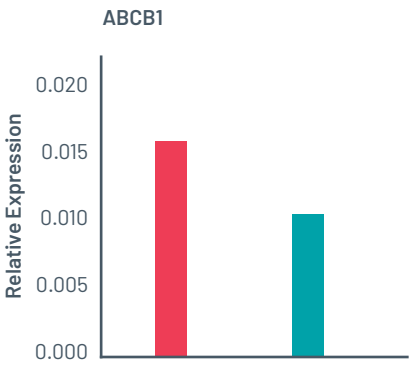

Figure 5. Def-INTESTINAL ABCB1 gene expression analysis. The analysis shows transporter ABCB1 expression profiles in the Def-INTESTINAL cells are similar to the primary human control.

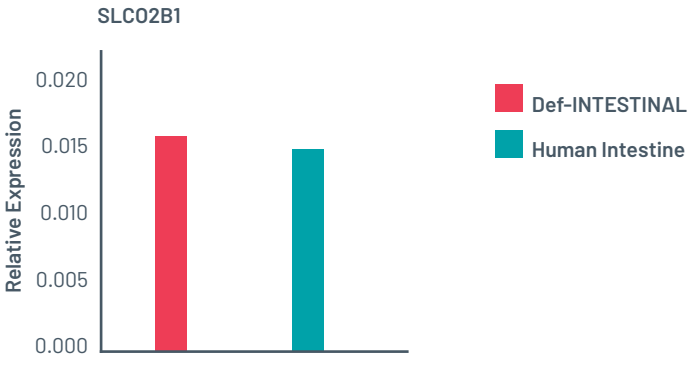

Figure 6. Def-INTESTINAL SLCO2B1 gene expression analysis. The graph shows transporter SLCO2B1 expression profiles are similar in both the Def-INTESTINAL cells and the primary human control.

Immunocytochemistry analysis

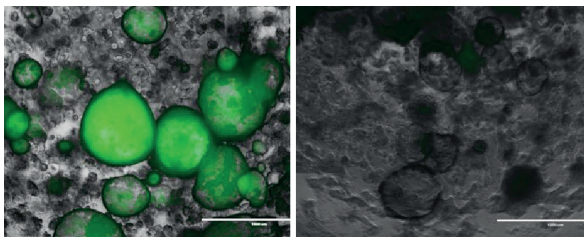

Figure 7.

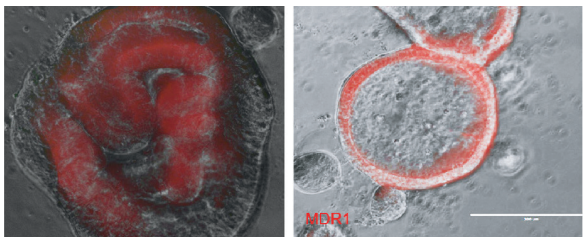

Figure 8.

Figure 7. Def-INTESTINAL MDR1 transporter analysis. Def-INTESTINAL organoids can transport Rhodamine 123, a specific substrate of MDR1. MDR1 activity is inhibited by Verapamil, a specific inhibitor.

Figure 8. Def-INTESTINAL MDR1 localization. Immunostaining of intestinal organoids showing localization of the MDR1 transporter protein within the highly folded crypt structures of the organoids.

Key References

Derivation of Intestinal Organoids from Human Induced Pluripotent Stem Cells for Use as an Infection System. Forbester JL, Hannan N, Vallier L, Dougan G. Methods Mol Biol. 2016 Aug 31.

Interaction of Salmonella enterica Serovar Typhimurium with Intestinal Organoids Derived from Human Induced Pluripotent Stem Cells. Forbester JL, Goulding D, Vallier L, Hannan N, Hale C, Pickard D, Mukhopadhyay S, Dougan G. Infect Immun. 2015 Jul;83(7):2926-34.

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