pixlbio

CASE STUDY

Decoding biology.
Pixel by pixel.

www.pixlbio.com

pixlbio iPSC-derived intestinal organoids (pixIO) for drug metabolsim, absorption and safety assessment

Drug-induced gastrointestinal toxicity is an underestimated adverse effect associated with a variety of symptoms ranging from asymptomatic histological changes in the gastrointestinal tissues to fatal complications. Alongside drug-induced liver injury, drug-induced gastrointestinal toxicity is a reason for drug discontinuation during drug development. However, and despite the severity of the problem, the mechanisms of drug-induced gastrointestinal toxicity are poorly understood, mainly due to the lack of relevant in vitro models able to recapitulate intestinal physiology. pixlbio intestinal organoids provide a unique in vitro system to model the human intestine. Our iPSC-derived organoids (pixIO) harbor a combination of cell types normally present in the primary intestinal epithelial **in vivo**, including goblet cells, Paneth cells, enterocytes, stem cells, and enteroendocrine cells. Our intestinal organoids models offer a suitable and physiologically relevant in vitro model for drug absorption and metabolism, efflux transporter studies, as well as the modeling of infectious diseases.

Document No 123456a

CASE STUDY

pixIbio intestinal organoids (pixIO) morphology

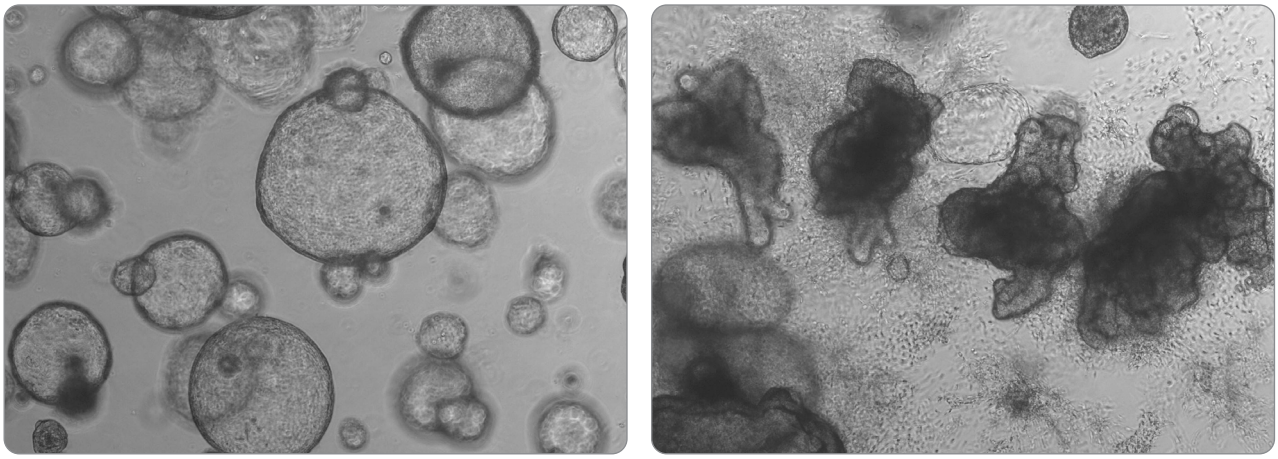


Figure 1. pixIO morphology after two (left) and eight (right) passages encapsulated in matrigel.

pixIbio pixIO expresses key intestinal cell markers at mRNA and protein level

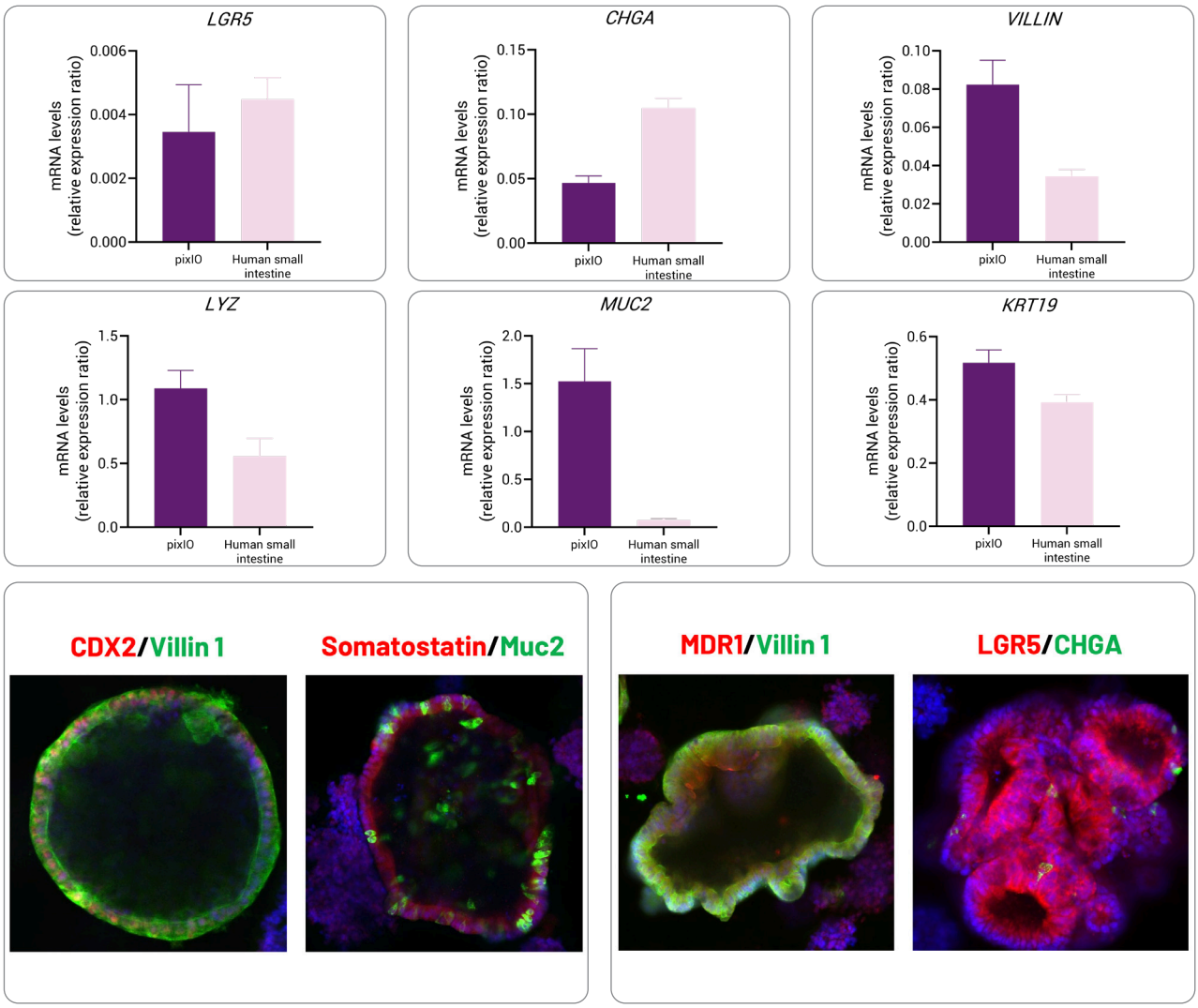


Figure 2. pixIbio intestinal organoids (pixIO) demonstrate comparable gene expression levels of key intestinal markers (LGR5, CHGA, VILLIN, MUC2, LYZ, KRT19) to human small intestine tissues (upper). pixIO express key intestinal protein markers present in different cell populations (enterocytes, Paneth cells, Goblet cells, enteroendocrine cells, stem cells) using immunocytochemistry. mRNA data were normalized to housekeeping gene GAPDH and are presented as mean±SEM of n=4 independent experiments.

Document No 123456a

pixIbio pixIO demonstrates a similar transcriptional profile to primary human intestinal tissues compared to carcinoma cell lines

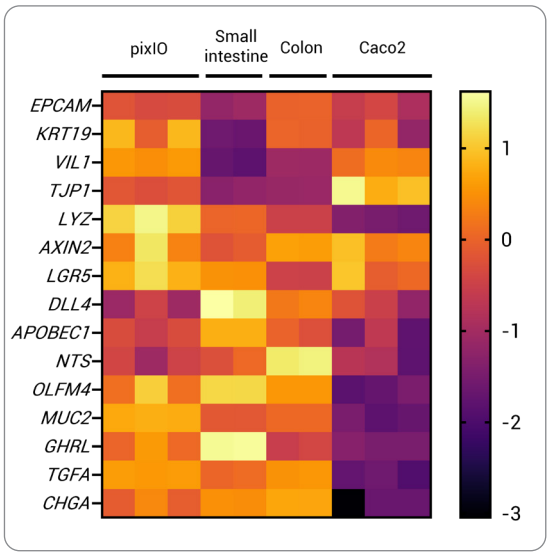
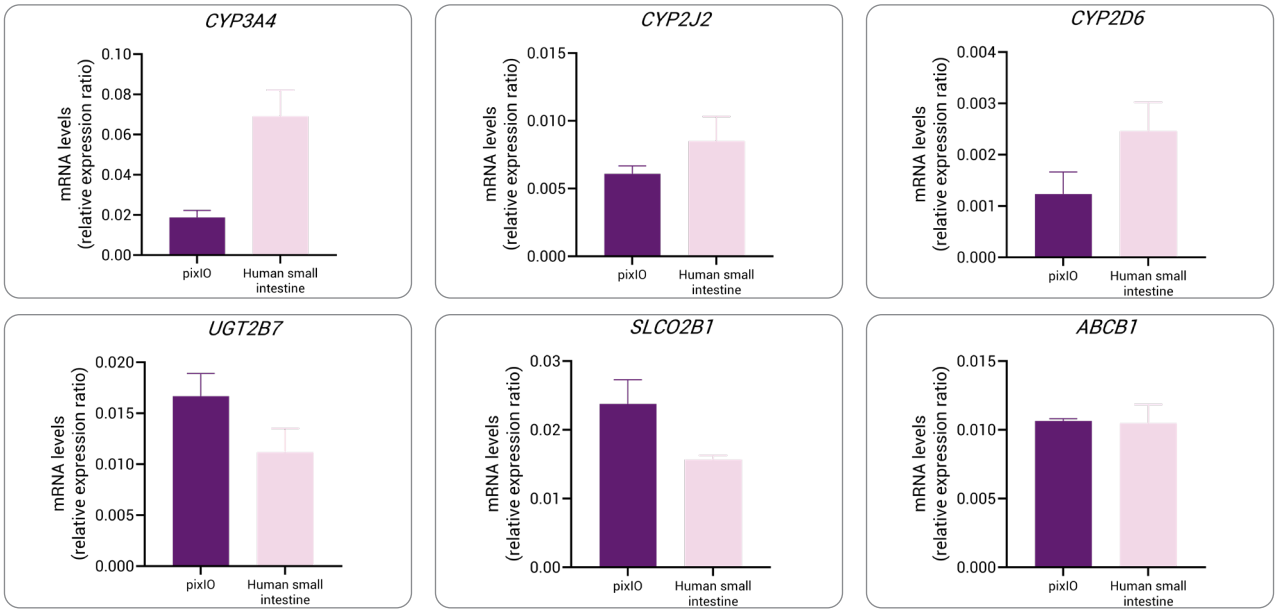


Figure 3. Heat map following bulk RNA-sequencing depicting the expression levels of key intestinal markers expressed in different cell populations (enterocytes, Paneth cells, Goblet cells, stem cells, enteroendocrine cells), revealing a similar transcriptional profile between pixIbio pixIO intestinal organoids, primary human small intestine, and primary human colon tissues. Distinct transcriptional differences are observed between the first three intestinal models and Caco2 carcinoma cells.

pixIbio pixIO expresses key drug metabolism and transporter markers



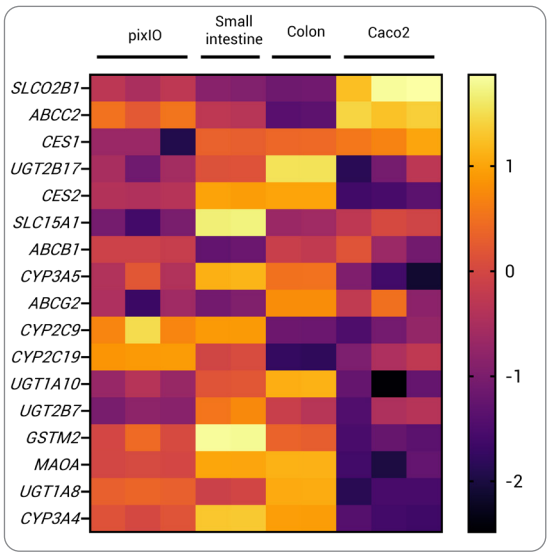
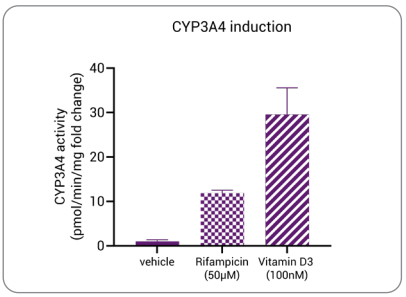
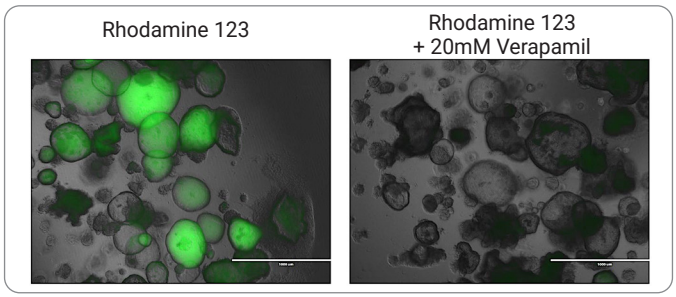


Figure 4. Heat map following bulk RNA-sequencing depicting the expression levels of key intestinal markers expressed in different cell populations (enterocytes, Paneth cells, Goblet cells, stem cells, enteroendocrine cells), revealing a similar transcriptional profile between pixIbio pixIO intestinal organoids, primary human small intestine, and primary human colon tissues. Distinct transcriptional differences are observed between the first three intestinal models and Caco2 carcinoma cells.

CASE STUDY

pixlbio pixIO intestinal organoids demonstrates functional CYP450 induction, detoxification, and transporter activity





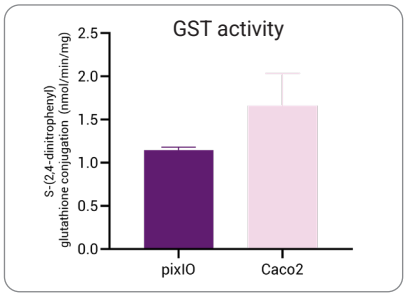


Figure 5. CYP3A4 mRNA induction in pixIO following 72 hours of treatment with vehicle, 50μM Rifampicin, or 100nM vitamin D3 (CYP3A4 inducers) (upper left). pixIO demonstrate functional MDR1 (ABCB1) activity following organoid treatment with Rhodamine 123 (MDR substrate; green), and this effect can be reversed following co-treatment with Verapamil (MDR1 inhibitor; 20μM) (right). pixIO intestinal organoids demonstrate functional detoxification pathways, as shown by comparable Glutathione-S-Transferase (GST) activity to that observed in colorectal adenocarcinoma Caco2 cells (lower left). Data are presented as mean±SEM of n=2-3 independent experiments

Advantages

Wild-type iPSC donors with normal human genetics and verified karyotype

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

Functional cells that can be used for drug absorption and metabolism, transporter induction, and infectious disease modeling

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

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

Document No 123456a