

# Human Intestinal Enteroids as a model for viral infection

Created on: 26-01-2023 - Last modified on: 27-01-2023

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## Organisation

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## SCOPE OF THE METHOD

<b>The Method relates to</b>	Human health
<b>The Method is situated in</b>	Basic Research, Translational - Applied Research
<b>Type of method</b>	In vitro - Ex vivo

## DESCRIPTION

### Method keywords

organoids

3D culture

ECM

Transwell

### Scientific area keywords

Intestinal organoids

gastroenteric viruses

gastroenteric infection  
viral infection  
co-culture

## **Method description**

Human Intestinal Organoids (HIOs) are *in vitro* 3D cell cultures arranged in a crypt-villus structure that incorporate many physiological features of the intestinal epithelium, including the presence of different cell populations (enterocytes, goblet cells, enteroendocrine and Paneth cells). HIOs can be generated from isolated crypts that contained the intestinal stem cells from small intestinal primary tissue (Enteroids) or they can be generated from pluripotent stem cells (Organoids). HIOs have emerged as a unique opportunity to study hard-to-cultivate enteric viruses *in vitro* and better understand their biology. We use human small intestine tissue-derived organoids (enteroids) that are 3D cultured in ECM (matrigel) in a growth medium rich in Wnt3, R-spondin and Noggin. For viral infection several approaches can be used a) differentiation of enteroids in 3D and infection with virus in suspension; b) seeding of enteroid single cell suspension in collagen coated plates or c) in transwell inserts that allow co-culture of these enteroids with other cells of interest (eg. Immune cells). The 3D infection of enteroids has been a successful model to evaluate the antiviral activity of compounds and an excellent opportunity to push antiviral drug discovery to the next level.

## **Lab equipment**

- Biosafety cabinet
- CO2 cell incubator
- Refrigerated centrifuge
- Microscope

## **Method status**

Published in peer reviewed journal

## **PROS, CONS & FUTURE POTENTIAL**

### **Advantages**

Enteroids preserve the degree and diversity of glycosylation on histo-blood group

antigens (HBGAs) of the donor patient, that is related to the activity of fucosyltransferase 2 gene (FUT2), a crucial genetic factor for susceptibility to some gastroenteric viruses like HuNoV and HRV, allowing for the first time the *in vitro* replication of some virus strains.

## **Challenges**

- Enteroids are composed of only epithelial cell types lacking complex mesenchymal heterogeneity and architecture, vasculature, neuronal connections and interaction with immune cells and the intestinal microbial flora.
- Organoid culture requires specialized training to manipulate ECM and due to ECM's characteristics automatization is difficult.
- Medium and related reagents are rather expensive.

## **Modifications**

- Co-culture with other cell-types is being explored.

## **Future & Other applications**

- Enteroids are currently being used as a model for antiviral drug discovery. Optimization of methods for higher throughput are ongoing.
- Further interaction with immune cells to study the epithelial immune barrier function in the presence of pathogens and co-culture with other organ-derived organoids will be studied.

## **REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION**

### **References**

Mirabelli C, Santos-Ferreira N, Gilliland MG 3rd, Cieza RJ, Colacino JA, Sexton JZ, Neyts J, Taube S, Rocha-Pereira J, Wobus CE. Human Norovirus Efficiently Replicates in Differentiated 3D-Human Intestinal Enteroids. *J Virol*. 2022 Nov 23;96(22):e0085522. doi: 10.1128/jvi.00855-22. Epub 2022 Nov 7. PMID: 36342297; PMCID: PMC9683019.

Zou WY, Blutt SE, Crawford SE, Ettayebi K, Zeng XL, Saxena K, Ramani S, Karandikar UC, Zchos NC, Estes MK. Human Intestinal Enteroids: New Models to Study Gastrointestinal Virus Infections. *Methods Mol Biol*. 2019;1576:229-247. doi:

10.1007/7651\_2017\_1. PMID: 28361480; PMCID: PMC5752619.

## Associated documents

[jvi.00855-22.pdf](#)

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