

Development of multi-organ-on-chip model to unravel gut-blood-cerebrospinal fluid-brain communication

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SCOPE OF THE METHOD

The Method relates to	Human health
The Method is situated in	Basic Research, Translational - Applied Research

Type of method	In vitro - Ex vivo
Species from which cells/tissues/organs are derived	human
Type of cells/tissues/organs	intestinal epithelial cells, choroid plexus epithelial cells, cortical brain cells

DESCRIPTION

Method keywords

gut-brain

microfluidics

Scientific area keywords

fatigue

inflammatory bowel disease

Method description

We established a human multi-organ-on-chip model to recapitulate key physiological elements of gut-brain communication via the systemic circulation and the blood-cerebrospinal fluid barrier (BCSFB). In our model, a gut-blood barrier, comprised of Caco-2 (enterocytes) and HT29-MTX cells (goblet cells), is connected to a BCSFB, composed of HIBCPP and iHCPEnC cells (choroid plexus (ChP) epithelial and endothelial cells respectively), and to a brain compartment (SH-SY5Y, neurons) via recirculation of cell culture medium.

Lab equipment

- QuasiVivo® 1200 (QV1200) platform (Kirkstall Ltd (York, UK)), compatible with Millicell® standing cell culture inserts (Ø 12 mm)

- Ismatec® Reglo ICC Digital 4 channel peristaltic pump, silicone tubing (Ø 0.8-2.26 mm) and Luer-lock connectors.

Method status

Still in development

PROS, CONS & FUTURE POTENTIAL

Advantages

Millifluidics allows to sample the cells for flexibility in downstream analysis. In addition, it reduces the air bubble clogging, mass transport issues with nutrients, oxygen and waste metabolites.

Challenges

- Leaks, contamination.
- No immune cells are included for now.
- No real-time monitoring of TEER.

Modifications

- Primary cells can easily be implemented (eg human gut organoids, and brain cells).
- 3D structures in the gut compartment will allow more physiological conformation.
- Immune cells could be included in the blood flow compartment.

Future & Other applications

The method is optimized for gut, cerebrospinal fluid, brain studies, that could be of interest in other diseases in which the gut-brain axis is implicated, such as Parkinson's disease, multiple sclerosis, depression)

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

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