



Patient derived rectal organoids (PDRO) and 2D monolayers from patient with Cystic Fibrosis

Commonly used acronym: PDRO

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Organisation

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SCOPE OF THE METHOD

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|---|--|
| The Method relates to | Human health |
| The Method is situated in | Basic Research, Education and training, Translational - Applied Research |
| Type of method | In vitro - Ex vivo |
| Type of cells/tissues/organs | Intestinal epithelial cells from human rectal biopsies |
| Specify the type of cells/tissues/organs | Intestinal epithelial cells from human rectal biopsies |

DESCRIPTION

Method keywords

Human Intestinal Organoid
3D culture
Transwell
drug repurposing

Scientific area keywords

cystic fibrosis
adult stem cells
epithelial cells
CFTR
Organoid biobank
Disease modeling
intestinal crypt

Method description

Adult intestinal stem cells are grown into closed 3D structures with protruding buds and a luminal compartment. These 3D structures are produced from the stem cells present in the base of crypts isolated from rectal mucosa samples that can be collected by suction or forceps biopsy. The crypts are cultured in extracellular matrix and using a multi-component media that allows fast proliferation of the stem cells as 3D structures; the so-called rectal organoids. This 3D epithelial model maintains disease and patient specific characteristics, thus can be used to evaluate CFTR function, predict responses to modulators, characterized CFTR rare mutations and help in unclear CF diagnoses. Additionally, rectal organoids can be dissociated, cultured as polarized 2D cultures on permeable plastic supports and used to measure transepithelial currents in Ussing chambers.

Lab equipment

- Biosafety cabinet,
- CO2 cell incubator,
- centrifuge,
- microscope.

Method status

Published in peer reviewed journal

PROS, CONS & FUTURE POTENTIAL

Advantages

- Organoids are patient-derived primary cells models that faithfully reproduce the subjects' genetic background.
- Organoid cultures can be bio-banked and expanded indefinitely.
- Can be used for personalized testing of responses to CFTR therapeutics as organoid-guided n-of-1' trial approach when traditional clinical trial are not possible due to the reduce number of patients with a specific CF genotype.
- Organoid assays have HTS capability.
- High Levels of CFTR protein in stem cells present in the crypts facilitate testing of efficacy of CFTR therapeutics.
- Isc measurements of polarized 2D cultures on permeable supports may overcome this limitation of ICM with tissues that requires instant analysis without excessive storage times.

Challenges

- Rectal organoids represent only epithelial cells from the intestinal tract present.
- Requires specialized training ECM and medium including growth factors is rather expensive.

Modifications

- Organoids can be cultured from other organs, like lungs.
- Development of more complex models including other cell-types.

Future & Other applications

Organoids biobanked can be used to test novel CF therapies developed in the future like gene therapies.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

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Links

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