

iPSC-derived Human Liver Organoid

- Preclinical tool for identifying an effective therapeutic agent in alleviation of liver injury and liver disease -



Summary of the inventions

- Drug-Induced Liver Injury (DILI) is a critical challenge in drug development.
- One major cause is drug-induced cholestasis by inhibition of transporter activity.

The Human Liver Organoid (HLO)

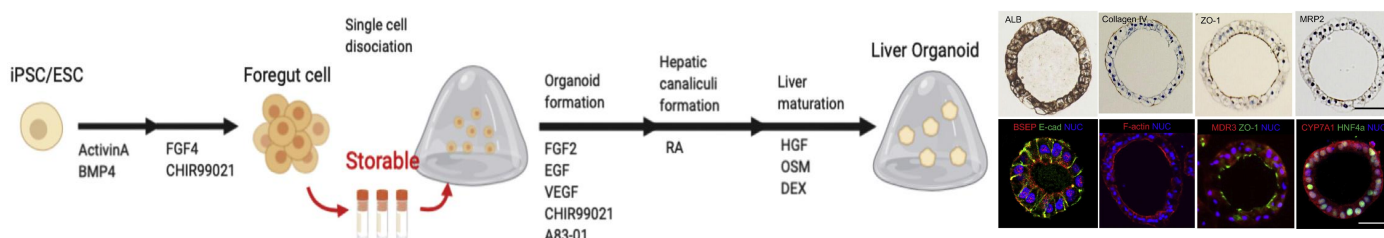
"A preclinical tool in identifying an effective compound with less DILI-like condition"

1. Human liver organoid

- Contact iPSC-derived definitive endoderm with;
1st step: **FGF pathway activator+GSK3 or Wnt signaling pathway activator**
2nd step: **retinoic acid**

2. Lipotoxic organoid model

- Contact a liver organoid with a **free fatty acid** (oleic/linoleic/palmitic acid)

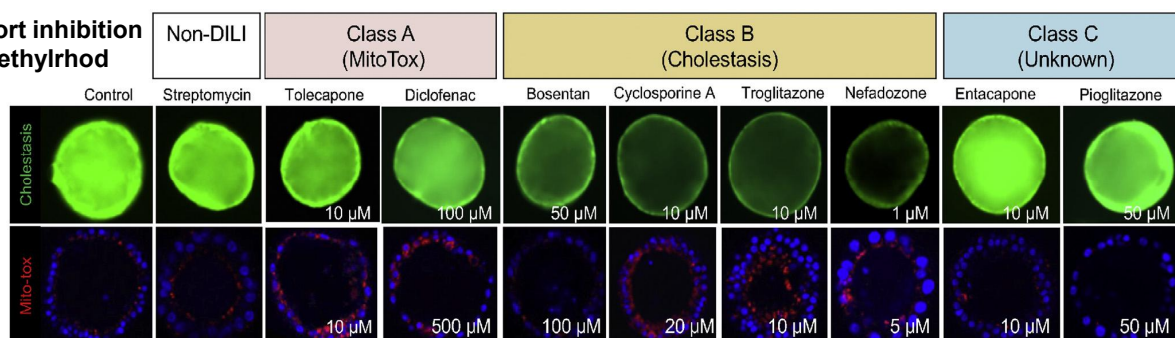


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HLO shows;

1. microvilli, intraluminal surface, bile canaliculi-like structure
2. ability to produce bile acid, uptake it from outside and efflux it inside HLO
3. Excellent predictability of CLF transport inhibition induced by cholestatic drugs; the sensitivity of 88.7% and specificity of 88.9%

Image of FD transport inhibition and MMP on tetramethylrhod

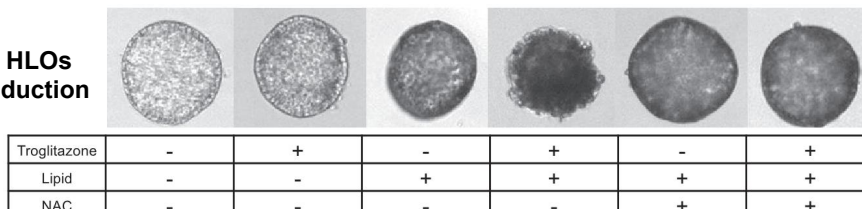


CLF: cholesteryl-luciferase-Fluorescein, FD: fluorescein diacetate, MMP: mitochondrial membrane potential

4. Lipotoxic HLO model possibly highlights DILI vulnerability.

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Rescued cell death in HLOs by inhibiting ROS production



ROS: reactive oxygen species, NAC: N-acetylcysteine

Major advantages of the patented technology

1. Use of patient's iPSC
2. Storable feature at foregut stage
3. High-throughput assay
4. Multiplexed readouts for analyzing interplay of factors (ex. mitochondrial stress)

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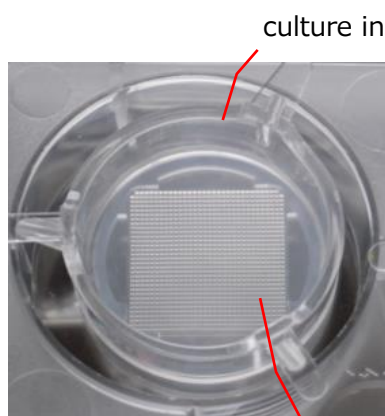
Three-Dimensional Cell Cultures microplate TASCL

In regenerative medicine, the usefulness of cell clusters (spheroids, embryoid bodies) by 3D culture is drawing attention. Microplate "TASCL" that can easily realize 3D cell culture and differentiation induction. This is a product with the following seven features developed by our original fine processing technology and surface treatment technology.

[7 features of TASCL]

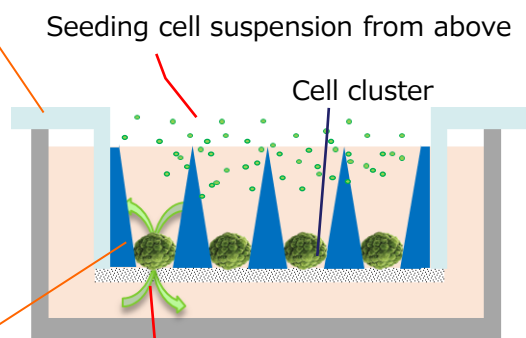
1. Massive cultivation of spherical 3D cell cluster of almost uniform size at one time (about 3600 or about 6000 in one set).
2. The state of the cells can be kept long and good ... because the bottom surface penetrates and the gas and medium circulate.
3. Differentiation can be induced ... Long-term culture for one month is possible.
4. Total cost can be reduced ... Small and dense well structure saves equipment, medium and reagents.
5. Can be used immediately after opening ... Anti-cell adhesion coating, and gamma ray 25kGy irradiation, set in advance.
6. Easy to use ... Just seed the cell suspension from above (no centrifugation required), easy medium exchange.
7. Easy to observe ... Microscopic observation of cells can be done on TASCL.

TASCL + culture insert

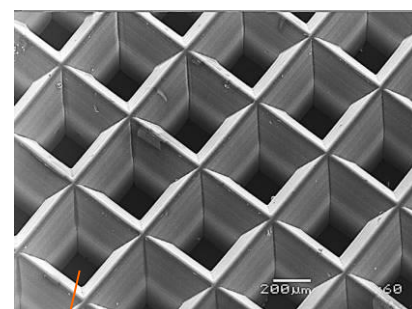


TASCL

Cross section during cell culture (image)



Enlarged photo of micro well



There is a through hole on the bottom of TASCL, and gas and medium circulate from the top and bottom of the well.

Models of TASCL

TASCL 1000 well

Number of wells 1020
Upper part of well
500μm × 500μm
Well bottom
250μm × 250μm
Well height 500μm
Estimated number of
cultured cells per well
500-3,000

TASCL 600 well

Number of wells 621
Upper part of well
650μm × 650μm
Well bottom
400μm × 400μm
Well height 500μm
Estimated number of
cultured cells per well
2,000-10,000

Open price. Please contact us.

TASCL one set



In one set, 6 culture inserts and 6 TASCLs are attached to a 6-hole plate, which is packaged after Anti-cell adhesion coating, and gamma ray 25kGy irradiation.