SACI Office of Society Academia Collaboration for Innovation
KYOTO UNIVERSITY

Liver-on-a-chip for Disease Modeling and Drug Screening

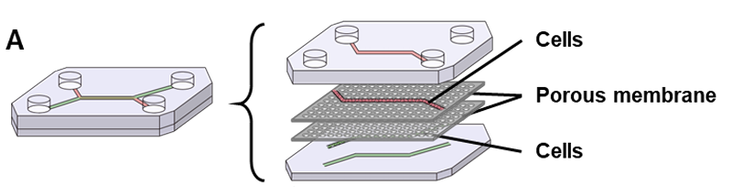
We are looking to out-license the technology for its commercialization

Background

Drug discovery is oftentimes hindered by inadequate disease models. For diseases affecting the liver 2D hepatocyte culture models are generally used which fail to recapitulate the organ functions and pathophysiologies. Organ-on-a-chip technique has recently gained attention for liver modeling, and several devices containing different liver cell types have been developed. The present invention is a liver-on-a-chip (LoC) device which contains hepatocytes and cholangiocytes (bile duct epithelial cells) therefore reproducing the hepatic region around the bile duct in 3D for the first time.

Technical Summary

The inventors developed a PDMS microfluidic device with two parallel microchannels separated by two PET membranes (**Fig.1A**). Hepatocytes are placed into the top channel and the bottom channel is seeded with either cholangiocytes or endothelial cells to reproduce the hepatic region around the bile duct (*ibd-LoC*) or blood vessels (*bv-LoC*) respectively (**Fig. 1B**).



	ibd-LoC	bv-LoC
Top channel	Hepatocytes	Hepatocytes
Bottom channel	Cholangiocytes	Endothelial cells

Figure 1

➢ Tubular bile duct-like structure is formed

The inventors have shown that the manufactured device can be used to obtain a tubular bile duct-like structure to accurately mimic the pathophysiology of the liver around the bile ducts. Previous attempts at reproducing tubular bile duct structures in vitro failed due to a technical difficulty of low migration rate of bile duct epithelial cells. The present device faithfully reproduces bile duct structure allowing the assessment of bile acid kinetics.

➢ Drug screening can be performed

PDMS microfluidic devices pose a concern of drug absorption which might hinder their utility for drug screening. The inventors developed a method to estimate drug-specific absorption of the device which shows that only drugs with high S + log D values are absorbed (Deguchi et al. 2021). They then applied several low S + log D drugs and confirmed that the device can successfully be used for small molecule drug screening (Deguchi et al. 2023).

Development Status

- Microfluidic device has been verified to be effective for modeling liver pathophysiology in COVID-19 and testing antiviral and immunosuppressive drugs

Applications

- Modeling of liver- affecting diseases
- Drug screening
- Pre-screening for minimizing drug-induced liver injury
- Toxicology tests

Intellectual Property

- Licensing
- Option to license (for feasibility study)

※Patent pending

Publications

Deguchi S, Kosugi K, Hashimoto R, Sakamoto A, Yamamoto M, Krol RP *et al.* Elucidation of the liver pathophysiology of COVID-19 patients using liver-on-a-chips. *PNAS Nexus* 2023; 2: gad029.

Deguchi S, Tsuda M, Kosugi K, Sakamoto A, Mimura N, Negoro R *et al.* Usability of Polydimethylsiloxane-Based Microfluidic Devices in Pharmaceutical Research Using Human Hepatocytes. *ACS Biomater Sci Eng* 2021; 7: 3648–3657.

SOCIETY ACADEMIA COLLABORATION FOR INNOVATION (SACI)
Kyoto University Division

215, 2/F, International Science Innovation Building
Kyoto University, Yoshida-honmachi, Sakyo-ku, Kyoto
606-8501 JAPAN

Email: gtcunit@mail2.adm.kyoto-u.ac.jp
Phone: +81-75-753-5692