Human Biomimetic System RIKEN Hakubi Research Team
RIKEN Hakubi Team Leader: Masaya Hagiwara (Ph.D.)

(0) Research field

CPR Subcommittee: Biology and Engineering

Keywords: In vitro tissue formation, Tissue imaging, Organ on a Chip, Culture Control

(1) Long-term goal of laboratory and research background

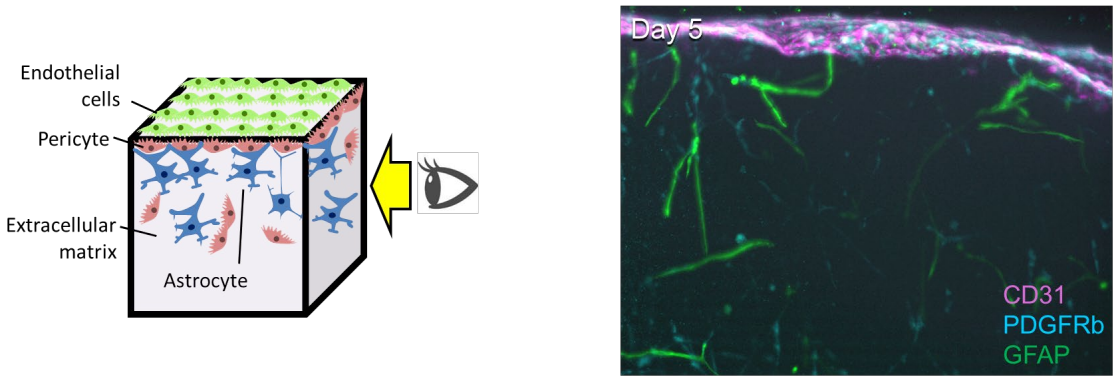
The overall objective is the development of in-vitro experimental platform to reconstitute the biological system outside our bodies by controlling cellular micro-environments. Especially lung airway is the one of my major targets. The scientific question is how the airway cells can organize such a sophisticated structure by themselves. The repetitive feedbacks between in-vitro experiments and mathematical model give us a tremendous amount of useful information, and I am challenging to unveil the system underlying self-organization of tissue formation by directing complex tissue structure. Development of Organ or Body-on-a-Chip system is another research target for the animal testing alternative.

(2) Current research activities (FY2019) and plan (until Mar. 2025)

A multicellular organization is a complex system and the mechanisms are poorly understood. The mathematical model could provide a powerful tool for elucidating the mechanism, but various mathematical models have been proposed for a single tissue formation because there is no evaluation. In this year, we have achieved to establish the system of assessing the validity of those mathematical models quantitatively. We have developed “in vitro-in silico interface platform” which performs repetitive feedbacks of in vitro results and in silico results. Controlling the initial conditions in vitro can reduce the experimental noise to improve the reproducibility of the developed pattern formation. Then, feature extraction of reproducible data of collective cells converts a large amount of data into the meaningful information. By comparing these features with in silico results repetitively, the mathematical model can be validated and optimized.

We have also developed the system for Organ-on-a-Chip, which emulates the circulating system in our body to express organs communications. A cartridge type microfluidic system to counter the complexity of the system in OoC has been developed. By employing the system, we can develop arbitrary combinations of multi-organ network with in a minutes.

For the future plan, we are going to develop time-lapse imaging system to measure cellular behaviour during tissue morphology. By rotating the cubic device automatically under a microscope, multi-directional imaging can be conducted so that fine imaging with large scale can be achieved. The new in-vitro model with barrier function will be also developed to be applicable for drug screening tests.



F i g . 1 3D blood-brain barrier model in a cubic device

(3) Members as of March, 2020

(RIKEN Hakubi Team Leader)
Masaya Hagiwara

(RIKEN Hakubi Team Leader)
Isabel Siew Yin Koh

(Technical Staff)
Ayane Kataoka

(Student Trainee)
Asuka Yamaguchi

(Assistant)
Izumi Arimitsu

(4) Representative research achievements

1. M. Hagiwara, I. Koh, "Engineering approaches to control and design the in vitro environment towards the reconstruction of organs", Dev. Gowth Differ., doi.org/10.1111/dgd.12647, 2020.
2. 萩原将也, "制御・計測・情報技術が繋ぐ多細胞システム解析", 生物物理, 60 ,pp19-24, 2020.
3. S. Mori, E. Sakakura, Y. Tsunekawa, M. Hagiwara, T. Suzuki, M. Eiraku, "Self-organized formation of developing appendages from murine pluripotent stem cells", Nat. Comm., 10, 2019.
4. M. Hagiwara, "Cube in a Chip: One touch 3D tissue integration and removal system for body on a chip platform", The 23rd International Conference on Miniaturized Systems for Chemistry and Life Sciences, 2019.
5. A. Yamaguchi, M. Akiyama, I. Nakase and M. Hagiwara, "In vitro-in silico interface platform: bridging the gap between experiment and theory by information system to elucidate cellular behaviour system", The 23rd International Conference on Miniaturized Systems for Chemistry and Life Sciences, 2019.

Laboratory Homepage
https://www.riken.jp/en/research/labs/hakubi/h_hum_biomimetic/index.html