

Report for Interdisciplinary research startup

1. Name of project leader : **Shinya Tanaka**
2. Project title: **Elucidation of reprogramming phenomenon into cancer stem cells using polymer hydrogel and establishment of new cancer stem cell targeted therapy**
(ポリマーハイドロゲルを用いたがん幹細胞へのリプログラミング現象の解明と新規がん幹細胞標的治療法の確立)
3. Report

We have previously found polymer hydrogels induce cancer cell reprogramming in a very short time to create cancer stem cells (CSCs) (Japanese Patent Application 2017-028833, PCT/JP2018/ 005884, US 16/487,247). Toward clinical application, we here analyzed the reprogramming induction phenomenon by hydrogels by combining computational science, information science, and experimental science of ICRéDD.

(i) Creation of reprogramming-guided hydrogel substrate (Fusion with Gong-G)

In order to efficiently induce reprogramming of cancer cells, we optimized the hydrogels by adjusting the elastic modulus and charge state. In addition, for rapid and efficient large-scale drug screening for CSCs induced by hydrogel, we succeeded in constructing a system that a sheet-shaped gel can be easily cut and installed into a 24-well plate. This is an extremely important technological innovation for "development of CSCs diagnostic kit using hydrogel".

(ii) Creation of reprogramming analysis platform by hydrogel (Tanaka-G)

To quantify spatiotemporal variables in hydrogel-induced CSCs formation, we performed scRNAseq of brain tumor cells cultured on hydrogels, and succeeded in identifying multiple markers specific for CSCs. This will be valuable information for the selection and creation of CSCs-targeting drugs, and also will be the basic knowledge for the creation of a new academic field called "Material Genomics" which is the ultimate goal of this project within ICRéDD project.

(iii) Creation of technology and theory for predicting and manipulating characteristics and dynamics of cell populations (Fusion with Komatsuzaki-G)

We are now developing a method for predicting CSCs transformation from spatiotemporal cell dynamics information based on information science methods, which makes it possible to predict the induction process of CSCs. In addition, we are constructing rapid drug screening technology with accuracy guarantee using Multi-armed Bandit algorithm. This enables rapid selection of CSCs-targeting therapeutic agents for clinical application.

Taken together, the results of these fusion research will lead to the development of CSCs diagnostic methods based on highly functional hydrogels and the creation of CSCs-targeting therapeutic agents as medical applications of the ICRéDD project.