# Laboratory of Cell Function Design

## **Institute for Protein Research**



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Living organisms are composed of various types of cells. Cells communicate with each other to self-organize and maintain complex tissue structures. Furthermore, tissues can adapt to environmental changes and regenerate after injury. Our goal is to understand the mechanisms of how cells generate tissue-level structures and functions and to develop new technologies for constructing synthetic tissues by design. In addition, we aim to develop molecular toolkits for manipulating cell behavior and engineering cell-cell communication rules in vitro and in vivo. By applying these technologies, we strive to propose novel therapeutic approaches for currently untreatable diseases.

#### Synthetic biology research to create and understand tissue-level dynamics and functions (Figure 1)

Cells regulate the behavior of each other by communicating with nearby cells through various types of chemical and mechanical signals. In our bodies, numerous reactions occur between cells simultaneously, making it difficult to understand the relationship of cellcell interactions and multicellular behavior. To address this challenge, we construct novel cellcell communication rules in cultured cells using molecular toolkits such as synthetic receptors and analyze emergent multicellular behavior. By this bottom-up approach, we investigate what kinds of cell-cell communication rules can generate multicellular structures and patterns. So far, we have found that we can reproduce various morphogenetic processes with synthetic cellcell communication mechanisms that regulate cell adhesion, cell death, and secretion of signaling proteins. Beyond understanding morphogenesis, we also explore how tissue functions such as homeostasis and regeneration can emerge in multicellular systems. By developing the methods to

manipulate cell behavior and cell-cell communication, we are tackling the fundamental question of biology: "How do molecular and cellular collectives become life"?

#### Development of "Designer therapeutic cell" to control tissue formation in vivo (Figure 2)

Using the technologies to manipulate cellcell communication, we aim to create "Designer cell" that can communicate with specific target cells and perform user-defined actions in our bodies. For example, we construct designer cells that recognize damaged tissues and produce factors for tissue regeneration and inflammation suppression. Through repeated cycles of design, build and validation, we assess whether these designer cells can treat and regenerate diseased tissues. We explore new therapies for inflammatory and degenerative diseases that are currently difficult to treat with conventional drugs by engineering cell-cell communication in vivo.

細胞間相互作用のデザイン



自己組織化する多細胞体の合成



パターン形成過程の再構成

赤色レポーターのみ 赤色+細胞接着の誘導





ばらつきを含む勾配

### 生体内での細胞間相互作用の操作



#### 潰瘍部位で機能する細胞医薬の開発



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