【Grant-in-Aid for Transformative Research Areas（A）】

Section III

Title of Project： Understanding multicellular autonomy by competitive cell-cell communications

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【Purpose of the Research Project】

A critical difference between multicellular living organisms and non-living thing is that the former has ‘autonomy’. A multicellular system can spontaneously construct tissues and organs and optimize its structure and function by itself. While the mechanism by which a cell population spontaneously creates a structure is gradually being clarified, the mechanism by which a cell population optimizes its own structure and function is still elusive. Recent advances in single-cell analysis technology have identified that there are ‘variations’ in various cell populations within the animal and that these variations are eliminated over time. In addition, when cells with slightly different properties or status (but viable on their own) are emerged in a cell population, such ‘unfit’ cells are actively eliminated from the population via cell-cell interactions, a phenomenon called ‘cell competition’. Thus, cell competition optimizes the structure and function of the cell population by excluding unfit cells. In this Research Area, we will approach one of the greatest mysteries of life, the multicellular autonomy, by studying competitive cell-cell communications (Fig. 1).

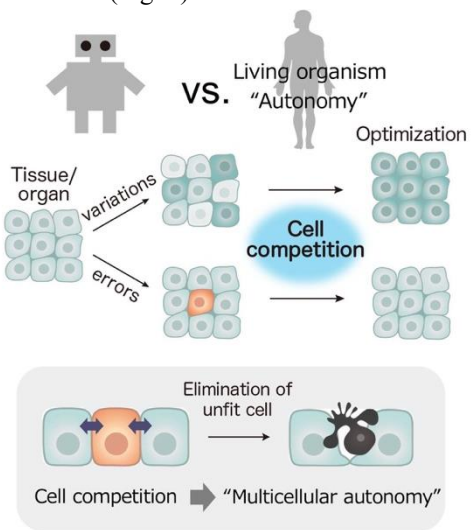

Fig. 1　Multicellular autonomy by cell competition

【Content of the Research Project】

We aim to elucidate the mechanism by which ‘autonomy’ is generated in multicellular systems by studying competitive cell-cell communications. To achieve this, we will study the molecular mechanisms of various competitive cell-cell communications and identify master regulators and specific markers for cell competition in various species and cell types. We will also capture, visualize, and control cell competition within animals and elucidate the roles and mechanisms of physiological cell competition. In addition, we will develop spatial multi-omics technology for competing cells within animals to greatly accelerate the Research Area. Furthermore, through the synthetic approaches to reconstruct cell competition and theoretical approaches to mathematically model cell competition, we will elucidate the universal mechanism of competitive cell-cell communication. Given that studying competitive cell-cell communication is not sufficient to understand multicellular autonomy, we will investigate the logic that each competitive communication generates multicellular autonomy: how the dynamics of cells that respond to changes and disturbances in a multicellular system optimize the system. By mutually feeding back the "molecular basis" and "multicellular autonomy" researches, we will achieve the goal of the Research Area. The following six subjects will be elucidated in the research period.

1. The cellular differences that induce cell competition
2. The core pathway of cell competition
3. Cell competition markers
4. The role and principle of physiological cell competition
5. Development of spatial multi-omics technology
6. The mechanism of multicellular autonomy

【Expected Research Achievements and Scientific Significance】

The mechanism of multicellular autonomy will be elucidated, which will open up a new field of life science that solves the principle of biological systems from competitive cell-cell communication and bring new perspectives and research styles to basic biology and medicine. Visualizing cell competition in animals and establishing methodologies to control cell competition will contribute to understanding various diseases such as cancer and providing new therapeutic strategies for them.

【Key Words】

Cell competition: Cell elimination via cell-cell interaction.
Multicellular autonomy: The property of the multicellular systems that spontaneously forms and optimizes its structure and function.

【Term of Project】

FY2021-2025

【Budget Allocation】

1,113,000 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.multicellular-autonomy.lif.kyoto-u.ac.jp