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

Gauguin Biology: Unraveling the Past, Present, and Future of Cells through Environmental Adaptation and Diversity Changes

Principal Investigator	Kumamoto University, Faculty of Life Sciences, Professor MOROISHI Toshiro　Researcher Number : 30647722
Project Information	Project Number : 24B303　Project Period (FY) : 2024-2026 Keywords : Cellular diversity, Environmental adaptation, Cell lineage, Intercellular communication

Purpose and Background of the Research

●Outline of the Research

The human body is composed of approximately 30 trillion cells, with over 200 different types. In recent years, advances in single-cell biology have revealed that even cells categorized as the same type exhibit diverse genetic activities and cellular behaviors, unveiling various individual characteristics within each cell (**Figure 1**). Such cellular diversity has implications for the entire life cycle, including growth, aging, and the onset of diseases, suggesting a significant transition period in the concept of cellular diversity in life science research. French painter Paul Gauguin famously questioned the meaning of life in his masterpiece "Where Do We Come From? What Are We? Where Are We Going?" Similarly, understanding the origins and destinies of cells from the perspective of diversity formation is essential. Thus, in this research group named "Gauguin Biology," efforts are made to develop research technologies enabling the recording of cellular dynamics and intercellular communication over time. This allows for the investigation of how individual cells adapt to and are selected within their surrounding environments, shaping the diversity of cell populations. The aim of this research is to understand multicellular organisms from the perspective of cellular diversity (**Figure 2**).

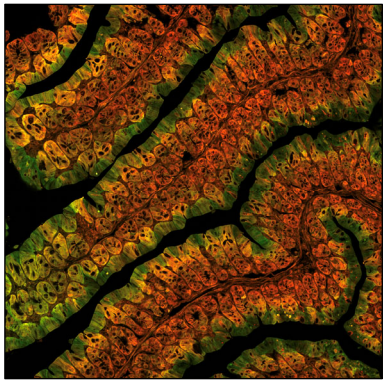

Figure 1. An example of cellular diversity observed in mouse colon tissue

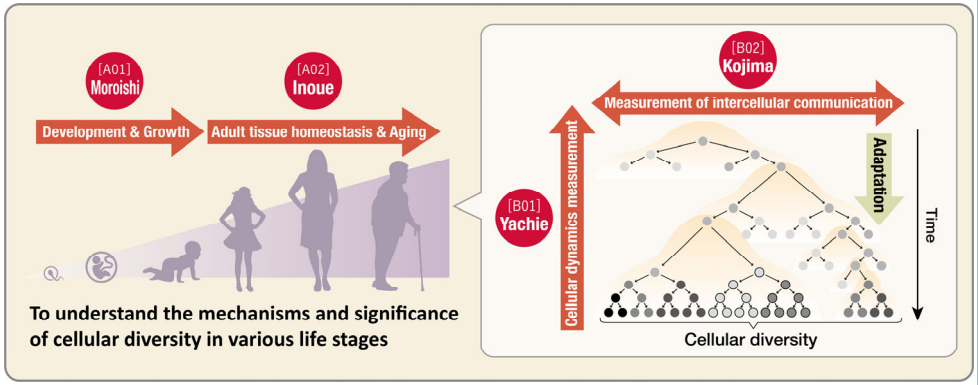

Figure 2. Outline of the research

●The goal is to understand "adaptive diversity"

In multicellular organisms, a single fertilized egg acquires diversity as a cell population through repeated division and differentiation, forming complex tissues. Darwin's theory of evolution suggests that organisms on Earth have evolved to adapt to various environments, thereby developing diversity. Similarly, it is anticipated that individual cells also change in response to their surrounding environment, forming cellular diversity, although the process is not fully understood. In this research group, we define the process of forming cellular diversity through the adaptation and selection of individual cells to the surrounding environment as "adaptive diversity". To establish the platform of research in "adaptive diversity", it is necessary to gather researchers from multiple disciplines such as genome engineering, molecular and cellular biology, and pathophysiology to conduct research that overlooks the formation of cellular diversity. We believe that this will break through the current technical constraints of life science research and significantly transform the concept of cellular diversity.

Expected Research Achievements

●Specific Aims (see **Figure 2**)

1. Recording of Cellular Dynamics:
To comprehend the mechanisms driving the formation of cellular diversity, it is crucial to monitor changes in cellular dynamics over time. [B01] Yachie group will employ a genome barcoding system to document cellular events within their DNA, thereby establishing a system to retrospectively construct cell lineages.

2. Understanding Cellular Diversity at Different Life Stages:
Utilizing the aforementioned techniques, we will investigate changes in cell lineages and diversity in response to environmental changes across various life stages of mice. [A01] Moroishi group will examine the formation of cellular diversity during development and growth. [A02] Inoue group will investigate the mechanisms and significance of "adaptive diversity" in adult tissue homeostasis and aging.

3. To Expand "Adaptive Diversity" Research:
Based on the techniques to track cell lineages retrospectively, a research methodology for capturing cellular dynamics will be established within this research group. These techniques will be shared with researchers outside to promote the expansion of "adaptive diversity" research. Additionally, [B02] Kojima group will develop a system to record intercellular communication, investigating the mechanisms by which specific cells expand or are eliminated during the transition of cellular diversity.

●Research Impact

The process by which individual cells adapt to their surrounding environment and form cellular diversity is indeed the fundamental operating principle of multicellular organisms. We believe that elucidating this process will contribute to the understanding of various biological phenomena and diseases. In addition to advancing developmental biology and stem cell research, the conceptual insights gained in this research are expected to have broad implications for other life science research focusing on multicellular organisms. Given that alterations in cellular diversity are widely observed in multiple diseases, such as cancer and age-related dysfunctions, the knowledge gained from this research holds the potential to open up new avenues for future development of preventive and therapeutic strategies for various diseases.

Homepage Address, etc.	https://gauguin.kumamoto-u.ac.jp