Research area in Strategic Objective *"Challenging to create suprabiological tissue "*

Creation of supra-biological tissues through understanding and control of multicellular dynamics.

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Overview

This research area aims to understand the dynamics between cell-cell or cell-extracellular environment interactions at the field where cells form structures and perform functions, and to develop techniques to control cells using artificial materials, in order to construct complex tissues with properties, functions and mechanisms that can only be achieved by combining biological and artificial materials.

Recent advances in metrology and biocompatible materials have enabled combining biological and functional materials. In this research area, by utilizing these technologies for integrating cell populations and artificial materials, and by measuring, predicting and controlling multicellular states, we challenge to understand fundamental phenomena in the field where cells structure and perform higher functions, such as cellular communication and cell-material interactions, by integrating biological and artificial materials. Moreover, by controlling and adjusting the existing functions of cell populations or imparting new functions, we attempt to create "supra living tissues" or to "go beyond conventional technologies" to get closer to biological tissues. Furthermore, research aimed at applications in fields such as agriculture and botany by using variety of materials including animal cells, is also included in the scope of this research area.

We intend to integrate various scientific technologies, such as material, life sciences, engineering, materials science and mathematical science, and are taking on the challenge of creating 'Supra-Biological Tissues' through full-fledged interdisciplinary fusion by circulating knowledge between fundamental understanding of cells, materials and technology and the design and construction of tissues.

Research Supervisor's Policy on Call for Application, Selection, and Management of the Research Area

1. Background.

In recent years, rapid progress has been made in the development of omics technologies for the comprehensive measurement of biomolecules and the visualization technologies of intracellular molecules, for accurately describing cells, which are a complex set of chemical reactions, using vast amounts of data. However, measuring, describing and predicting the behavior of heterogeneous cell populations remains a challenging topic and, due to its broad applicability, is an area of research in which there is fierce international competition. Japan has produced many pioneering results in the field of stem cells and also has international advantage in the field of materials. Research based on a manufacturing approach has also traditionally attracted many researchers. While Japan has these unique advantages, fusion research in these different fields has not been active internationally. Against this background, the main objective of this research area is to train and produce internationally leading researchers in the field of "multicellular regulatory science", which is a true fusion field of biology and engineering, and we seek ambitious and unique research proposals.

2. Principle of invitation project and selection

The aim of this field, "Creation of supra-biological tissues through understanding and control of multicellular dynamics", is to control the behavior of cells (includes animal cells, plant cells, unicellular organisms such as bacteria) based on knowledge of complex principles of multicellular dynamics, and to create "supra" biological tissues with new functions. To achieve this, we welcome the following research proposals that will lead to the establishment of the new interdisciplinary field of "multicellular regulatory science" through the cycle of development, elucidation and application below to deepen knowledge.

-Development: technologies for multimodal measurement of heterogeneous cell populations, technologies for engineering and controlling biological tissues, new functional materials suitable for controlling cell populations, and mathematical and modelling methods for describing and predicting the behavior of complex cell populations.

-Elucidation and application: elucidation of the cellular or molecular mechanisms that control the diverse self-organizing phenomena that occur in cell populations through interactions between cells and with extracellular substances, and application of these technologies and knowledge.

The following are specific examples of research proposals for reference purposes, but they are only intended to give you an idea of what we are currently envisioning. As this Strategic Objectives is expected to be applicable to wide research fields, we look forward to encountering innovative proposals that we might not have imagined.

(1) Construction of tissue equivalent to living organisms

- Development of organoid technology with complex functions using stem cells, especially tissue induction technology that enables cells derived from multiple germplasms to differentiate simultaneously to perform functions more similar to organs.
- Development of bioprinting technologies for creating higher functional tissues.

(2) Construction of completely new tissues in which biological functions are adjusted and manipulated.

- Research on the development of devices that construct hybrid tissues with higher functions by combining biological tissues and artificial materials, and research on the adjustment and manipulation of molecular mechanisms that control biological functions.
- Research proposals on the construction of cell populations with higher functions using synthetic biology.

(3) Construction of new dynamic material systems using cell populations

- Proposals for the development of new technologies such as sensors and any research that will contribute to future diagnosis and drug development by utilizing cell populations that exhibit specific functions and combining them with artificial materials.
- Development of living materials with higher functions that can only be achieved by combining them with biological tissues..
- Development of composite materials such that the artificial material and cell populations exhibit self-organizing behavior as a single unit through interaction.

(4) Fundamental understanding and modelling of biological tissue control mechanisms, etc.

- Research that will lead to technologies for constructing tissues with more advanced functions in the future through the elucidation of biological tissue control mechanisms observed in specific life phenomena such as morphogenesis and pattern formation.
- Development of mathematical and modelling techniques that can predict the behavior of complex cell populations.
- Research that describes the state of cell populations from measurement data and enables prediction and control through modelling, as well as empirical research on this.

(5) Research and development of elemental technologies

- Research on the development of devices that can control the behavior of cell populations.
- Development of engineering technology that enables real-time measurement, prediction, and feedback control of the differentiation state and behavior of cells in tissues to guide the cell population towards the designed state.

3. Research periods and research funds

In principle, the research period is 3.5 years, and the total research budget is maximally 40 million yen (direct costs).

4. Principle of research-area management

As this research area is based on the fusion of biology and engineering, we intend to rally researchers in different fields within the area. We will also actively interact with the research supervisor, research area advisors, and CREST researchers of the CREST "Supra-biological Tissues" area, and promote the development of cross-disciplinary fusion research. As the PRESTO project supports individual-type research, it is ideal that researchers with expertise in multiple fields actively make proposals in this area and promote fusion research on their own, but we do not exclude researchers who are currently experts in one field but who intend to boldly dive into a different field in the future. In your proposal, please specify how your research could be developed by incorporating research from a specific different field after the proposal has been accepted.