Research area in Strategic Objective “Challenging to create suprabiological tissue”

Creation and novel function development of supra-biological tissues through interdisciplinary fusion

Research Supervisor: Kazunari Akiyoshi (Professor Emeritus/Project Professor, Graduate School of Medicine, Kyoto University)

Overview

This research area explores supra-biological tissues, defined as tissues wherein the intrinsic functions of living organisms are either enhanced, diminished, or newly introduced to specialize or adapt to specific functions. Our endeavor involves the creation of supra-biological tissues through various combinations of biological and synthetic materials.

In detail, we aim to construct high-functioning, high-quality tissues with functionalities, morphologies, or polarities equivalent to those found in living organisms. We also focus on the design and control of cell population composition and organization to create dynamic material systems that exhibit specific functions. To realize this vision, it is crucial that manufacturing research and the understanding of phenomena and principles interact in a mutually reinforcing manner. Incorporating new ideas, concepts, and technologies that transcend traditional disciplinary boundaries is essential. In this research area, we promote research with a dual focus on practical applications across a wide range of fields and free and unrestricted basic research, through interdisciplinary integration and researcher connections. We also work on understanding and modeling the regulatory mechanisms of biological tissues, such as intercellular communication, as well as the combined dynamics of materials/devices and cell populations. Additionally, we develop new enabling technologies to support these efforts.

Innovative technologies and new insights created in this area are expected to bring innovation to the fields of bio and life sciences, materials science, and medicine, etc.

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

1. Background

In recent years, there has been significant attention on the development of technologies that merge the adaptability and higher-order functions inherent in biological materials with the stability and ease of design and control characteristic of artificial materials. From a practical application standpoint, there is an expectation to generate entirely novel technologies from our country to ensure international superiority. Our nation has a strong presence in fields such as iPS cell and stem cell research. Efforts in related studies aim to construct tissues akin to living organisms, such as organoids; however, these endeavors remain in a developmental stage. Conversely, rapid advances in measurement, analysis, and control technologies—incorporating recent AI developments—along with progress in Bio-DX research, gene editing technologies, and synthetic biology have propelled technological innovation in life sciences related to understanding, predicting, and controlling biological phenomena. Consequently, achieving a complex and hierarchical understanding of biological phenomena, ranging from the molecular to cellular and tissue levels, is becoming increasingly feasible. Moreover, as the sophistication of bio-adaptive material design, self-organization, various engineering technologies (such as MEMS and 3D fabrication), along with mathematical and information technologies continues to advance, a robust foundation is being laid for creating more functional and higher-quality tissues.

Based on the aforementioned situation, this research area seeks to challenge the creation of supra-biological tissues by exploring tissues with enhanced or diminished inherent functions of living organisms, or tissues specialized or adapted by adding new functions. By integrating various scientific and technological disciplines, we aim to establish a research domain that fosters technological innovation originating from our country and drives global advancements. Through these efforts, we aspire to bring transformative innovation to the fields of bio and life sciences, materials science, and medicine. Additionally, we aim to contribute to the resolution of social issues such as environmental purification, resource recycling, food security, and health and medical problems, thereby facilitating the transition to a sustainable society.

2. Principle of invitation project and selection

In this research area, we strive to create new tissues— supra-biological tissues —that surpass biological materials and exhibit properties, functions, and mechanisms

unattainable through artificial or biological materials alone. This is achieved by integrating various scientific and technological fields, including life sciences, medicine, medical engineering, biomaterial engineering, pharmacy, biotechnology, materials science, polymer science, mathematical sciences, information sciences, physics, chemistry, botany, and agricultural science. Our goal is to foster innovation in bio and life sciences, materials science, and medical fields. To this end, we will drive research and development based on the following three components:

① Creation of new tissues with adjusted or manipulated biological functions:

This component focuses on creating tissues with enhanced or diminished functions of biological control systems as well as tissues specialized or adapted with added new functions. The creation of innovative tissues and new functions inspired by various biological tissues and biological functions, for example, systems that regulate and control biological functions such as immunity, development and regeneration, neurology, metabolism and endocrinology, as well as sensory functions of living tissue (e.g. vision, hearing, touch) are expected. Moreover, it includes biotechnological and synthetic biological methods, such as genetic function modulation and artificial cellular organization, to harness and utilize the latent potential abilities inherent in living organisms.

② Creation of functional tissue equivalent to living organisms:

By developing and utilising material and device technologies, it is envisaged that technologies that can control the differentiation and organisation of stem cells and iPS cells and their functions will be created, and that tissues with morphology and functions equivalent to various biological tissues (epithelial tissue, connective tissue, muscle tissue, cranial nerve tissue, bone tissue, etc.) that were previously difficult to create will be created. The following methods are used to control the differentiation and organisation of cells. Possible methods for controlling cell differentiation and organisation include, for example, morphological control using material and device technologies and hierarchical spatiotemporal response control of extracellular information (physical (mechanical, electrical, etc.) and chemical information and biological information). The creation and use of innovative organoid and organ models is expected.

③ Designing and constructing new dynamic material systems utilizing the higher-order functions and adaptability of cell populations:

This component involves creating and utilizing dynamic material systems that exhibit specific functions by designing and controlling the composition and organization of cell populations. It encompasses cell populations from unicellular organisms like microbes and bacteria to multicellular organisms (animals, plants, algae, fungi), and includes both

homogeneous and heterogeneous cell populations. Dynamic material systems that combine the advantages of artificial and living cells are expected to be applied to the systems, for example, to optimize manufacturing and circulation of materials, energy conversion, healthcare devices and sensors, and environmental purification systems through controlled functional expression in response to environmental changes or by self-repair and self-propagation.

As the process or result of these studies may lead to the creation of novel entities not existing in nature and possible extensions or modifications of biological functions (including human bodies), it is also expected that consideration will be given to appropriate information dissemination from the perspective of ELSI/RRI.

As a foundational support for these manufacturing research efforts, the following two elements are indispensable. Their mutual circulation and synergistic effects are expected to lead to the elucidation of new phenomena and principles and the creation of innovative technologies, thereby being jointly promoted:

④ Fundamental understanding and modeling of biological tissue control mechanisms, interactions between materials/devices and cell populations, and interfacial science
⑤ Development of enabling technologies for tissue creation, measurement and evaluation, and functional control

When proposing to this research area, it is required to integrate at least one of the three components and one of the two elements into an interdisciplinary research team. While points of consideration for the three components have been provided, proposals are not strictly limited to these points. Furthermore, we encourage active engagement in inter-team exchanges and collaborative research within the research area by sharing knowledge and technologies and receiving feedback.

3. Research periods and research funds

The research period should not exceed five years and six months (2025 – 2030 fiscal year).

The maximum budget for a research project is 300 million yen at the beginning (direct expenses). Please submit your application after carefully examining the amount appropriate to the size of your research team and the amount necessary to achieve the proposed content. Please note that the research budget may be adjusted upon selection as a result of close examination by the research supervisor.

The research budget will be reviewed on an annual basis. As a result of the review, the

research budget may be increased or decreased to reflect the progress of the research. After selection, an interim evaluation will be conducted in the fourth fiscal year of the research. Depending on the results of the evaluation, we may revise the research budget or request a reorganization of the research team.

4. Points to Note in Proposals

(1) Clearly Indicate Target Components: Please specify which of the three components your proposal addresses. Additionally, clarify the technological challenges that serve as bottlenecks in the implementation of your proposal, and provide specific and quantitative information on the superiority of your solutions over existing technologies, milestones for achieving solutions, preliminary examination results on feasibility, and backup plans to enhance the reliability of your technological development.

(2) Clearly Specify Included Elements: Regarding the included elements (at least one of the two), clarify the novelty and scientific and technological impact within each specialized field. Also, describe the target application and expected ripple effects when the proposed technology or findings are applied and implemented.