

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

Section II



Title of Project : Bottom-up creation of cell-free molecular systems: surpassing nature

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Number of Research Area : 21A205 Researcher Number : 50362653

【Purpose of the Research Project】

In this Research Area, we aim to construct molecular systems which have capabilities that exceed those of natural cells, or that natural cells do not possess, from the bottom up. Outcomes of this research will have applied and social impacts, *e.g.*, material production, drug discovery, measurement technology, environmental and energy technology, *etc.*

Research on the bottom-up creation of cells has progressed substantially around the world, resulting in reconstituted molecular systems that mimic various cellular functions and properties. However, the bottom-up construction of molecular systems aimed at applied and socially relevant goals has seldomly been pursued. Moreover, there are a limited number of examples of constructing molecular systems from the bottom-up which utilize the concept of Darwinian evolution to screen for an optimal combination of multiple components among various combinations, suggesting that research which incorporates continuous trials followed by selection may dramatically improve bottom-up research outcomes.

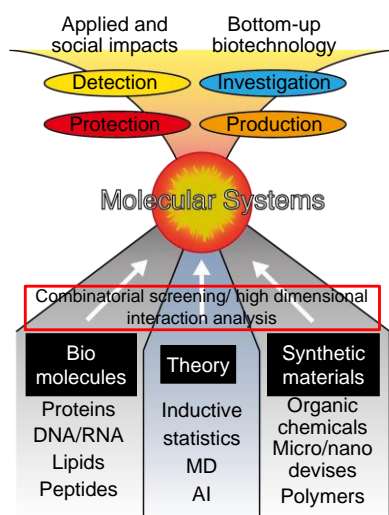


Figure 1: Schematic of the Research Area

In this Research Area, we define cell-free molecular systems as those constructed from defined molecules and materials from the bottom up, without using cells themselves as components. To construct cell-free molecular systems that can contribute to practical and applied goals, we will combine biomolecules, organic compounds, polymers, and micro- and nano-devices, while utilizing theoretical studies (Fig. 1). In addition, we will search for optimum combinations of components, as nature has done

in the course of Darwinian evolution and elucidate the interactions among the components. In this way, we will construct molecular systems which are highly functional by virtue of evolved interactions, and simultaneously systematize the methodology to create such systems.

【Content of the Research Project】

To achieve the goal, we will construct molecular systems which have applied and social impacts as listed below.

- Artificial cell sensor for ultra-sensitive detection of biomarkers and virus.
- Reconstituted virus- and bacteria-like particles
- Cell-free molecular systems that enable evolution that cannot occur in nature
- De novo cell membrane based molecular systems
- Enzyme embedded nanogel-fiber created by nanofluidic devices
- Computational science-based "optimal" cell-free molecular systems

In addition, we will elucidate the theory that can be utilized in the construction of these systems.

【Expected Research Achievements and Scientific Significance】

Through this Research Area, we expect to construct molecular systems that will contribute to various applications and social implementation. In addition, we will quantify the interactions between components and materials in the process of constructing cell-free molecular systems from the bottom up. This will lead to the understanding of the interactions among the constituents of the molecular system. This theory obtained in this area will serve as a guideline for the construction of new molecular systems.

【Key Words】

Cell-free science, synthetic biology, molecular systems, bottom-up biology, interaction, combinatorial screening

【Term of Project】 FY2021-2025

【Budget Allocation】 1,133,300 Thousand Yen

【Homepage Address and Other Contact Information】

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