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

Section II

Title of Project： Superior Protein Engineering by Evolution and Design

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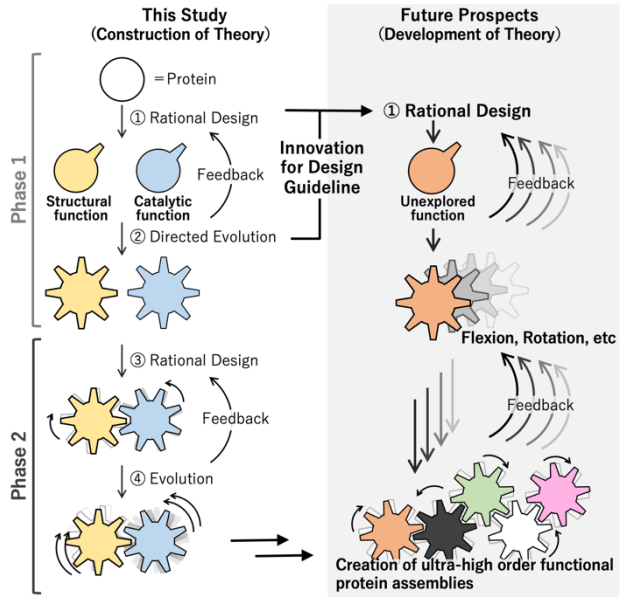
【Purpose of the Research Project】

The purpose of this project is to establish "Superior Protein Engineering by Evolution and Design (SPEED)," integrating the following three cutting-edge technologies in protein engineering: structural function design, catalytic function design, and molecular evolution.

Phase 1 of SPEED is the creation of functional proteins that surpass nature-derived proteins by combining rational design and directed evolution. Phase 2 is to construct functional protein assemblies that combines functional proteins from Phase 1 (See figure below). Then, we will rationalize processes of molecular evolution, giving us new insights for rational design. SPEED will develop a non-equilibrium system enabled by the cooperation of mesoscale structural change and catalytic chemical transformation which is difficult to realize with individual protein engineering approaches.



【Content of the Research Project】

Phase 1: Creation of functional proteins

Two groups, A01 and A02 will share "a stretchable protein" as a template protein, allowing integration of straightforward structure and catalytic function to achieve "non-equilibrium protein assembly" as mentioned above.

Group A01 will rationally design protein assemblies which is capable of controlling mesoscale structural changes by external stimuli. Group A02 is to develop activity switchable artificial enzymes. Concurrently, Group A03 will develop an infinitesimal high-speed directed evolution system of a higher-order protein complex (containing unnatural amino acids) utilizing a microdevice to drastically enhance the designed functions made by groups A01 and A02.

Phase 2: Creation of higher order functional protein assemblies

After developing SPEED Phase 1, we will merge protein assemblies that exhibit mesoscale structural changes constructed by groups A01 and A03 and activity switchable artificial enzymes created by groups A02 and A03 to construct "non-equilibrium system, the cooperation of mesoscale structural change and catalytic chemical transformation."

Through these approaches we will establish our state of art design, SPEED.

【Expected Research Achievements and Scientific Significance】

Our proposed approach on protein design SPEED, which integrates the three cutting-edged methodologies, will not only give a significant impact on protein engineering, but will be beneficial for various research fields outside of protein engineering; e.g. controlling cellular function by higher-order functional protein assemblies, construction of artificial cells, and self-healing of biomaterials. Protein-based material development can be considered as a desirable material for a sustainable society which is derived from biomass and have environmental degradability.

【Key Words】

Protein Design: Designing protein functions and structures.

Rational Design: A methodology in protein engineering to rationally design "catalytic functions" and "structural functions" based on structural information of proteins.

Molecular Evolution: A cutting-edge technology in protein engineering, a 2018 Nobel Prize award in Chemistry. A technology that dramatically enhances protein function by introducing multiple mutations into the enzyme.

【Term of Project】

FY2021–2023

【Budget Allocation】

105,000 Thousand Yen

【Homepage Address and Other Contact Information】

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