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

Development of next-generation pharmaceuticals through evolutionary engineering of precision polymers

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Research Area Information	Number of Research Area : 22B208　Project Period (FY) : 2022-2024 Keywords : Precision polymers, synthetic polymer pharmaceuticals, coevolution, uniform polymers

Purpose and Background of the Research

●Outline of the Research

The creation of new drug modalities is required in order to deal with the soaring prices of biopharmaceuticals and unmet medical needs (Figure 1, left). Synthetic polymers are promising as next-generation drug modalities because compound libraries with astronomical diversity can easily be synthesized just by designing and combining functional monomers. However, synthetic polymers have hardly been used as drugs due to concerns about their functions and side effects derived from heterogeneous molecular weights and monomer sequences. Recently, progress in polymerization and purification techniques for polymers enables synthesis of polymers with completely defined molecular weight and precise monomer sequences. In this project, we organize a research group by fusing scientists in the field of precision polymer synthesis with that of directed molecular evolution, high throughput screening, and computer modeling and simulation. A platform for developing precision polymer medicine, a next-generation drug modality, will be emerged as an outcome (Fig. 1, right).

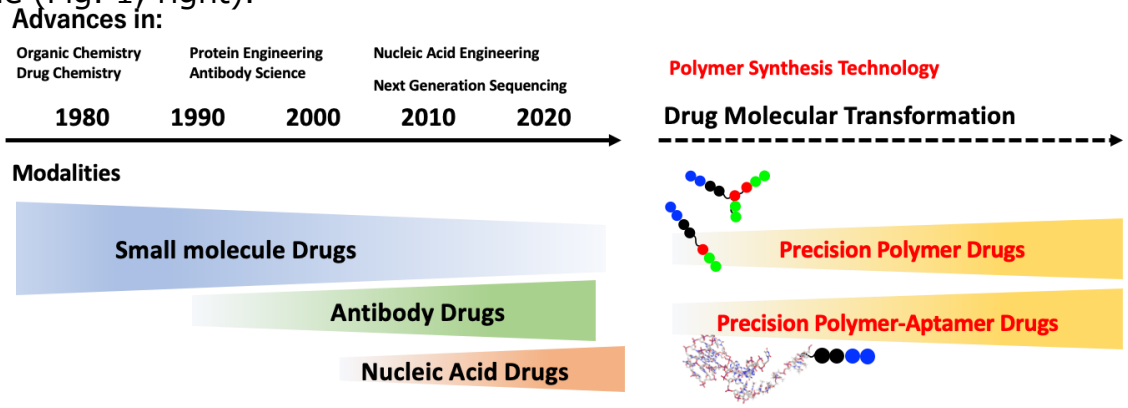

Figure 1. History and future direction of technology advances in the field of medicinal chemistry and drug modality

●Specific aimes

As a catalyst to create a platform for developing precision polymer medicine, a next-generation drug modality, a research group in the field of precision polymer synthesis (Hoshino group, Kyushu University), two research groups of directed molecular evolution (Yoshimoto group, Tokyo university and Sawada group, Tokyo institute of technology), and a research group in the medicinal chemistry (Koide group, University of shizuoka) collaborate for the first three years (Fig. 2). Specifically, we will achieve the following three specific aims within the research period.

Aim 1: Development of precision polymers that recognize target proteins and demonstration of disease treatment in animal models
Aim 2: Development of a high-speed evolution system for precision polymers
Aim 3: Development of synthetic/biopolymer pairs that recognize each other through coevolution of synthetic/biopolymers

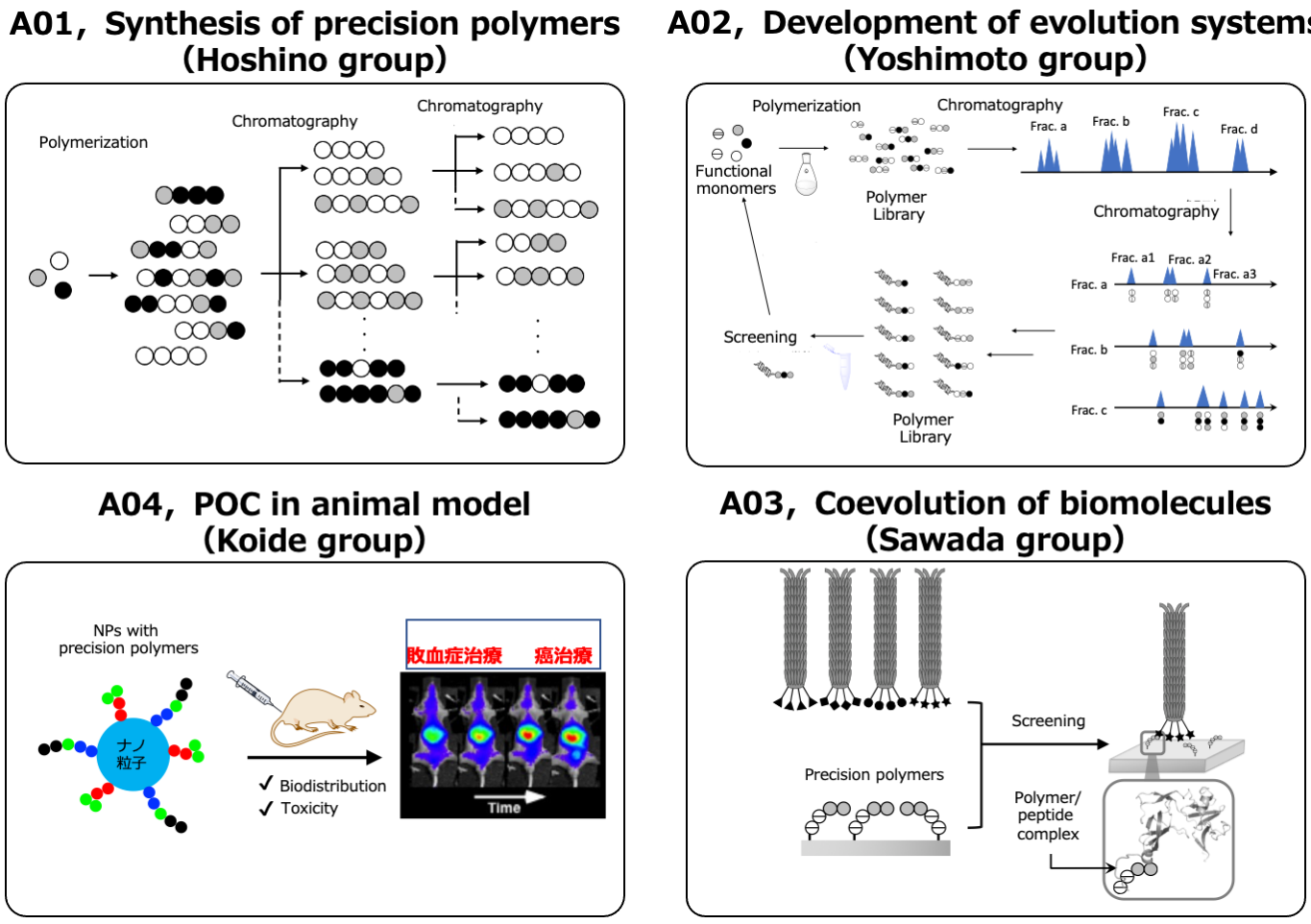

Figure 2. Outline of this project

Expected Research Achievements

In this project, four research groups will conduct research that will serve as a catalyst for building the platform for developing precision polymer medicine over a period of three years. After this project, a research area will emerge with researchers in the fields of precision polymer synthesis and biopharmaceutical drug discovery (Fig. 3 left). As a synthesis route for precision polymers, not only radical polymerization but also various polymerization methods such as the polycondensation method that has been developed in recent years will be included. It is also important to develop techniques for analyzing the sequences and structures of precision polymers and procedures for purifying the polymers. High-throughput screening techniques using microarrays, beads, and tags are required to achieve high-speed polymer evolution. Techniques that use structure-activity relationship databases and molecular dynamics calculations to find optimal structures in a short time from a large amount of interaction data will also be introduced. Collaborating with computational and computer scientists to fuse experimental and computational science is thus essential. For the co-evolution of biomacromolecules that recognize precision polymers, technology to create nucleic acids, peptides, and antibodies that recognize precision polymers is required. In order to realize precision polymer medicine, proof of concept and clinical research of precision polymer medicine will be conducted with specialists in not only cancer and sepsis but also immune diseases, infectious diseases, diabetes, etc. As described above, after the three-year project, precision polymers will be realized as a next-generation modality together with scientists representing various research fields.

Homepage Address, etc.	http://polymer-shinka.org