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

Drug development through data-driven evolutionary engineering of precision polymers

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Project Information	Project Number : 25A204　Project Period (FY) : 2025-2029 Keywords : Precision polymer, controlled polymerization, synthetic polymer pharmaceuticals, coevolution, material digital transformation

Purpose and Background of the Research

●Outline of the Research

The development of novel drug discovery modalities is urgently needed in response to unmet medical needs and the rising costs of biopharmaceuticals (Figure 1, left). Synthetic polymers, which allow the facile construction of highly diverse compound libraries through copolymerization of a wide variety of functional monomers, have long been regarded as promising next-generation drug modalities due to their cost-effectiveness and structural stability. However, most conventional synthetic polymers exhibit heterogeneity in molecular weight and monomer sequence, leading to inconsistent functionality. As a result, concerns over side effects have hindered their recognition as viable drug modalities, and there have been very few cases of their clinical application.

Recent advances in polymerization and purification technologies have enabled the synthesis of polymers with precisely controlled molecular weights and sequences, known as precision polymers. Precision polymers have been shown to exhibit specific antigen recognition capabilities.

We aim to create a new interdisciplinary research area by integrating expertise from the rapidly evolving fields of precision polymer synthesis, interaction analysis, and structural analysis with data science—including computational chemistry, machine learning, and bioinformatics—and materials informatics platforms (Figure 1, right). In addition, we will work closely with researchers in pharmaceutical development—such as those specializing in chemical biology and directed molecular evolution—to integrate these approaches. Concurrently, we will conduct proof-of-concept studies using animal models in collaboration with researchers involved in pharmaceutical development and clinical practice, ultimately constructing a platform capable of continuously generating precision polymer-based therapeutics.

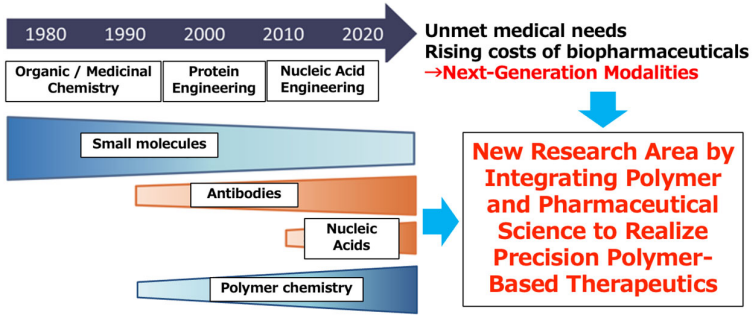

Figure 1.（Left）Recent trends in drug discovery modalities (Right) Core technologies in this Research.

●Positioning of This Research

The history of therapeutic antibodies is a history of antibody homogenization. Over the century following the discovery of antibodies, Nobel Prize technologies were developed almost every decade, ultimately enabling the mass production of entirely homogeneous, highly functional antibodies with minimal side effects, "humanized monoclonal antibodies"—thus realizing antibody-based therapeutics.

Meanwhile, in synthetic polymers, the concept of controlled polymerization was proposed in the 1980s, followed by the discovery of the controlled radical polymerization process in the 1990s, enabling precision polymer synthesis. In recent years, the advancement of purification and analytical technology enabled the isolation and characterization of uniform polymers. Furthermore, the MEXT Data Creation and Utilization-Type Material Research (Materials DX) platform accelerates the development of polymer-based therapeutics.

Expected Research Achievements

●Exploring Next-Generation Therapeutics with Precision Polymers

The research team has already been developing a method for synthesizing multifunctional uniform polymers and a screening system for polymers and has proved the concept of using synthetic polymers as an antidote in vivo. In this study, we incorporate data science for the evolution of polymeric drugs. Researchers in the synthesis, structural analysis, and assay of precision polymers will collaborate with researchers in the Materials DX Platform and combine this with drug discovery technologies such as in silico drug discovery and directed molecular evolution to revolutionize existing concepts and create new science. At the same time, we will work with clinical researchers to advance empirical research using model animals, creating a platform that will produce precision polymer medicines one after another.

To achieve this goal, the Polymer Chemistry Research Group (Yu Hoshino, Kyushu University), Data-Driven Evolution Research Group (Munehito Arai, University of Tokyo), Molecular Evolutionary Engineering Research Group (Keitaro Yoshimoto, University of Tokyo), and Drug Discovery Research Group (Hiroyuki Koide, Shizuoka Prefectural University) will work together to conduct core research in a new research field. Specifically, the following goals will be achieved within the research period.

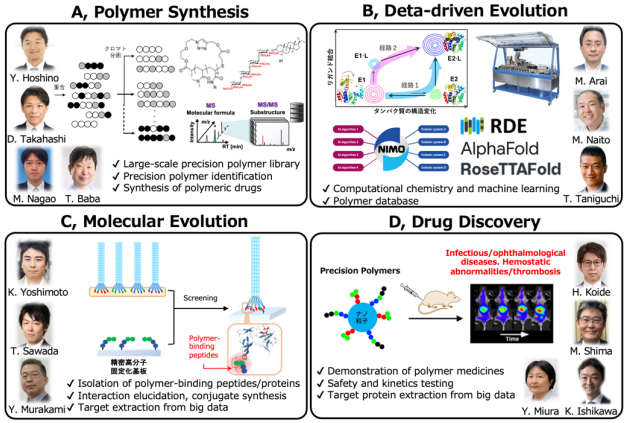

Figure 2. Research teams

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