Title of Project: Molecular design of innovative drugs based on molecular assembly

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Research Project Number: 19H05458  Researcher Number: 90198309
Keyword: Molecular assembling drug, Antioxidant, Parkinson disease, Oligo-nucleic acid, Cancer

【Purpose and Background of the Research】
Administration of conventional antioxidants such as vitamins and N-acetyl cysteine distribute nonspecifically and a serious disadvantage of destroying redox reactions in normal cells because of small molecules. We found that covalent attachment of antioxidants to macromolecules with self-assembling property suppresses uptake into normal cells and accumulates at inflammatory sites to effectively eliminate reactive oxygen species (ROS). This result indicates the possibility that the self-assembly of small molecules can realize pharmacological functions and therapeutic effects that cannot be obtained by small molecules alone. In this research, we develop a new drug discovery principle that exerts drug effects by self-molecular organization as a third drug modality, next to a conventional low molecular weight drugs and protein drugs. The results of this research are expected to be the foundation of innovative pharmaceutical industry and lead to the creation of patient-friendly medical technology.

【Research Methods】
This project is aimed at establishment of the concept for the molecular-assembling-drugs. Although amino acids and peptides show various physiological activities, and thus they are useful, they are water-soluble and rapid to metabolize and are difficult to carry and use to the target site. We have recently designed polypeptide based nano-assembles, which are stable under physiological conditions. After accumulation of the polypeptide in target site, it is metabolized to original amino acid by endogenic enzymes and functions as peptide drug. In addition to our original antioxidant self-assembling drugs, we will investigate versatile self-assembling drugs such as amino acids, fatty acids. Other types of molecular-assembling drugs such as the smart oligonucleotides incorporating a non-reactive molecule into the oligonucleotide, which can be activated by forming the hybridized complex with the target DNA or RNA. Self-assembling peptide derivatives that cause gelation at an extremely low concentration in a cancer cell, lead to selective cancer cell death. These new concepts will also be constructed.

【Expected Research Achievements and Scientific Significance】
Numerous numbers of synthetic drugs have been synthesized by organic synthesis for over 100 years. With the development of biotechnology in recent years, drug discovery is shifting from organic synthesis to biopharmaceutical synthesis. Based on such a paradigm shift, drug discovery technology has dramatically advanced and an extremely large market is anticipated, but due to protein engineering the cost of drug development is abnormally rising.

Unlike organic synthesis and biopharmaceuticals, the development of molecular assembling drugs is expected as a new drug discovery field (Fig.). As Japan is pioneering in the materials nanotechnology field, it is extremely important for us to develop a future academic field and create a new drug discovery field that does not follow the other countries. To discover new drugs and develop new medicine fields, it is important to take our own methods and way.

【Publications Relevant to the Project】

【Term of Project】FY2019-2023
【Budget Allocation】481,700 Thousand Yen

【Homepage Address and Other Contact Information】
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