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

Section IV

Title of Project： Synergy pharmaceutical science: understanding and design of compound combination effects by integrating information, material, and life sciences

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【Purpose of the Research Project】

Chemotherapy that utilizes the synergistic effect of a combination of multiple drugs (drug synergy) has been recognized as an effective method for treatment of multifactorial diseases such as cancer and neurodegenerative diseases. In addition to enhancing the therapeutic effect, it has the advantages of reducing the amount of individual drugs and reducing the frequency of serious side effects. However, since irrational drug combinations lead to harmful side effects, it is necessary to identify the optimal drug combination, which is extremely difficult. To date, many of the drug synergies have been discovered accidentally in clinical studies, and the molecular mechanism of disease-specific drug synergies is not well understood. Drug synergies are involved in the interaction between drugs and biomolecules, but the relationship with drug synergies is unclear.

In recent years, in the fields of material science and life science, various big data on genes, proteins, drugs and compounds (e.g., genome, omics, combinatorial chemistry) have been generated and accumulated. On the other hand, in the field of information science, the development of artificial intelligence (AI) and machine learning technologies is remarkable. In this research, we advocate a new academic field called "synergy pharmaceutical science" that systematically studies drug synergies, and aim at understanding of drug synergistic effects and construction of design methods through the collaboration of information science, material science, and life science.

【Content of the Research Project】

The "synergy pharmaceutical science" advocated by this research will be a new academic area created by connecting the fields of life science and material science through big data analysis by AI in information science. Bioinformatics for AI analysis of biomolecular data, chemoinformatics for AI analysis of drug/compound data, medical data analysis, organic chemical synthesis, and biological experiments will be performed. Our research team consists of three groups: AI group, medical data group, and pharmacology group.

In the group A01 (AI group), we will extend the technology of the machine learning method for predicting the target molecule and new efficacy of the drug to the combination of drugs, and develop new machine learning methods for predicting the combination of drugs and synergistic effects in this study. In addition, we will develop a mathematical model of the combination problem of drugs and biomolecules and its theoretical solution. Furthermore, the chemical structure of compounds with synergistic effects is predicted and designed.

In the group A02 (medical data group), we will analyze medical big data and develop data mining technologies for predicting drug pairs and drug combinations that have a disease-preventing effect.

In the group A03 (pharmacology group), we will construct pathological models for verifying the synergistic effects of the predicted drug synergies, and confirm the predicted pharmacological actions experimentally at the cell level and animal level.

【Expected Research Achievements and Scientific Significance】

To date, drug synergies have been discovered by chance in clinical studies. In this study we use AI to explore all possible combinations of drugs, which could solve the problem of combinatorial explosion.

Drug synergies are analyzed with respect to disease-specific abnormal expression genes and drug-responsive abnormal expression genes. Since drug synergies may be caused by the result of dynamic reactions in biological systems, the use of omics data will lead to accurate understanding of drug synergies.

Drug synergies are actually used in medical treatment in the form of multidrug therapy, but the drug selection criteria depend largely on the experience and knowledge of doctors and on the type of disease and the pathology of the patient. In this study, we can innovate the concept of polypharmacology by establishing a new strategy based on drug synergies supported by scientific evidence.

Many modern diseases such as cancer and dementia are multifactorial diseases, and the therapeutic effect is weak by single drug administration alone. Therefore, multidrug drug therapy is expected to be useful. The number of cancer patients in Japan is 890,000, and the number of dementia patients in Japan has reached about 4.62 million as of 2012. The results of this research can contribute to medical treatment.

【Key Words】
Drug synergy: Synergistic effects of combining multiple drugs

【Term of Project】 FY2020-2022

【Budget Allocation】 119,700 Thousand Yen

【Homepage Address and Other Contact Information】
http://labo.bio.kyutech.ac.jp/~yamanif/synergy/