【Grant-in-Aid for Specially Promoted Research】

Science and Engineering

Title of Project： Protein Encapsulation by Synthetic Cages for Functional Control and Structure Determination

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Research Project Number：19H05461　Researcher Number：90209065
Keyword：Protein encapsulation, NMR structure analysis, X-ray structure analysis, self-assembly, cage compounds

【Purpose and Background of the Research】

The principal investigator (PI) has pioneered a variety of self-assembled hollowed complexes and created a number of new scientific concepts related to the functions of their inner nanocavities since 1990. In this project, we aim to explore the potential of proteins encapsulated within precisely designed molecular capsules. More accurately, we will develop our technology based on the following perspectives: 1) control the property of protein (e.g., stability, ligand affinity or selectivity), 2) control enzymatic reactivity (e.g., activity or new function) and furthermore 3) develop new analytical methodology (coupled with NMR, X-ray, MS or cryoEM etc.). We envision to contribute to the field of life science by providing them the preceding fundamental technologies.

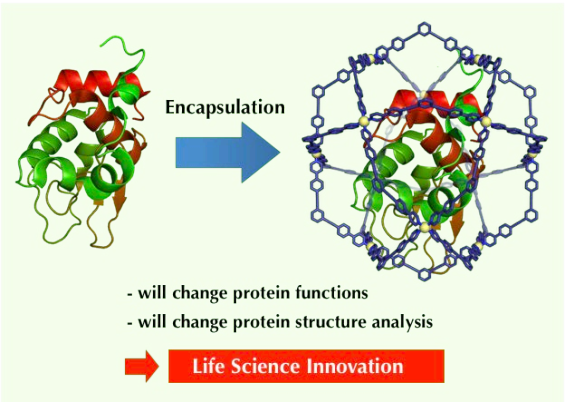

Figure 1. The basic concept of the project

【Research Methods】

We have already developed a mathematical design theory for the self-assembly of gigantic cage without critical upper size limits. Based on this theory, we further scale the size of synthetic molecular capsules. Basic methods for protein encapsulation in the cages have been also established. We are particularly interested in applications of the protein encapsulation that aids protein structural analysis. There still be many limitations in conventional protein structural analysis. Protein encapsulation in this study has the potential to solve some of the problems. As specific research projects, we will work on a) NMR data acquisition under non-biological conditions, b) Structural analysis of agglutinative proteins/peptides stabilized by encapsulation, c) Dynamic structural change analysis of proteins as typified by the folding process and d) New methodologies for facile X-ray or CryoEM structural analysis.

【Expected Research Achievements and Scientific Significance】

Taking the privilege to be the first one to explore this area of protein spatial modification, we are confident to unveil many fruitful results benefit multiple fields that handle protein molecules either in academic or industry. The true importance and necessity should accompany the following points: 1) the research stands on applicant's original science, 2) the research is not on the simple extension of the past, 3) no other groups has the similar research direction and 4) massive academic impact to be expected when it gets materialized.

【Publications Relevant to the Project】

・Self-Assembly of Tetravalent Goldberg Polyhedra from 144 Small Components, D. Fujita, Y. Ueda, S. Sato, N. Mizuno, T. Kumasaka, M. Fujit, Nature 2016, 540, 563-566.

・Protein encapsulation within synthetic molecular hosts, D. Fujita, K. Suzuki, S. Sato, M. Yagi-Utsumi, Y. Yamaguchi, N. Mizuno, T. Kumasaka, M. Takata, M. Noda, S. Uchiyama, K. Kato, and M. Fujita, Nature Commun. 2012, 3, 1093.

【Term of Project】FY2019-2023

【Budget Allocation】480,000 Thousand Yen

【Homepage Address and Other Contact Information】

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