Press Release

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Keio University
Shinshu University

Creating Nanoscale Soccer Ball-shaped Molecules with Proteins

—New Hollow Nanoparticles with Potential Applications in Nanomaterial Parts and Drug Delivery Capsules—

A research group including Assistant Professor Norifumi Kawakami and Professor Kenji Miyamoto of Keio University's Department of Biosciences and Informatics, Faculty of Science and Technology and Associate Professor Ryoichi Arai of Shinshu University's Department of Applied Biology, Faculty of Textile Science and Technology successfully constructed a soccer ball-shaped protein nanoparticle designated "TIP60" through self-assembly of building block protein molecules. TIP60 is a homogeneous hollow spherical supramolecule designed to have a diameter of about 22 nm. It was found that small organic compounds could be introduced into the internal cavity of TIP60 and that TIP60s could be further aggregated to create a larger structure. This achievement is expected to contribute to developments in nanotechnology through its application as drug-delivery nanocapsules or nanoblocks for creating nanomaterials with new structures.

The outcomes of this research were published in the September 17 issue of *Angewandte Chemie International Edition*.

1. Main Points of Research

- Creation of artificial fusion proteins by connecting two types of natural proteins.
- Self-assembly of 60 artificial fusion proteins into a hollow truncated icosahedral molecule (TIP60).
- Introduction of small compounds into the internal cavity of TIP60.
- Aggregation of TIP60 molecules to create a larger structure.

2. Background of Research

Nanoparticles are fascinating materials with applications expected across a broad range of fields including use as coloring agents, catalysts, and drug carriers. For practical applications, it is necessary to form numerous nanoparticles with uniform size and shape. Up to now, the formation of nanoparticles with metals as source materials has been extensively studied, while the formation of nanoparticles with uniform shape and size has been possible. Yet, even though these nanoparticles may be homogeneous, as individual nanoparticles are formed by random aggregations of atoms, it is not easy to create nanoparticles with the same structure at the atomic level. Therefore, this research group focused on proteins of biopolymers which fundamentally have the same structure at the atomic level. By utilizing proteins, the properties of nanoparticles can be freely transformed through gene mutagenesis or chemical modification, leading to the possibility of imparting desired functions and properties to the nanoparticles. Hence, it was

thought that it would be possible to develop groups of homogeneous nanoparticles with greater ease than using metal atoms. In this research, in addition to designing and constructing protein nanoparticles, methods for chemical modification of TIP60 and for the construction of even larger structures through further aggregation of nanoparticles themselves were developed.

3. Content of Research and Results

Protein nanoparticles that self-assemble from 60 artificial fusion proteins were designed. As shown in Figure 1, the pentagonal pentamer proteins (top left) and dimer proteins (top right) are artificially connected (top center). It is designed such that 60 of these artificial fusion proteins created by connecting the two types of proteins self-assemble with each other, finally becoming a soccer ball-shaped nanoparticle. When these artificial fusion proteins were purified and observed under an electron microscope, as well as through small-angle X-ray scattering analysis, it was found that nanoparticles with diameters of about 22 nm had formed as designed. The soccer ball-shape is a polyhedron called a truncated icosahedron, and this nanoparticle formed through the assembly of 60 artificial fusion proteins was named Truncated Icosahedral Protein of 60-mer fusion protein (TIP60).

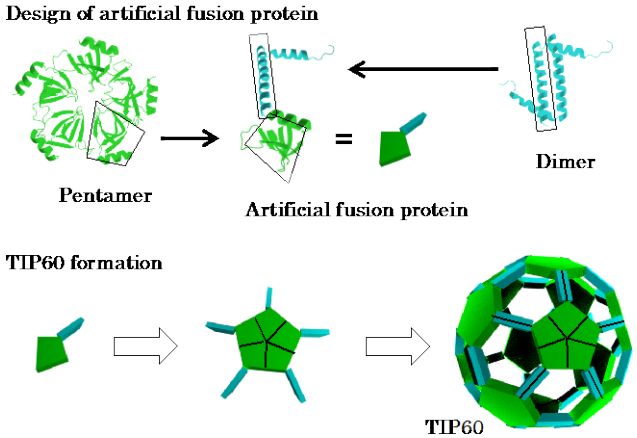

Figure 1: Design of artificial fusion protein (top row) and formation of TIP60 (bottom row)
Top left: Pentamer protein, Top right: Dimer protein
Top center: Artificial fusion protein
The monomer units to construct a fusion protein are framed in boxes.

As shown in Figure 1, TIP60 has an internal cavity and a large number of openings on its surface. In fact, when small compounds were added from the outside, they entered the internal cavity and chemically modified its inner surface. There are expectations of applying this characteristic of TIP60 to drug delivery systems.

In addition, another property of TIP60 is that it has negative charges as a whole, and by adding a material with a positive charge to it, TIP60s are further aggregated. Analysis of the aggregation process revealed that TIP60s do not randomly clump together, but follow certain rules. There are expectations that this could be used in the future to construct much larger molecular structures.

4. Future Developments

At present, the chemical modification of the inner surface of TIP60 has been carried out successfully. If a mechanism that allows for the release of the small molecules introduced into the inner space could be formulated, it could lead to the development of a useful drug delivery capsule. Furthermore, the property of TIP60 that allows it to systematically aggregate with one another may lead to the possibility of creating materials that are around 100 nm to 1,000 nm in size, which are difficult to produce using conventional methods, and there are expectations that it would become the next generation supramolecular nanomaterials.

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＜Details of Original Paper＞

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＜Glossary＞

※1 Nanoscale
Scale used to measure items typically between one-millionth and one-ten-thousandth of a millimeter

※2 Nanoblock
Nanoscale building-block molecules

※3 Artificial fusion protein
A single molecule protein created by connecting multiple proteins through genetic engineering

※ Please direct any requests or inquires to the contact information provided below.
※ This news release has been dispatched to the MEXT Press Club, Science Press Club, and the science departments of other media outlets.

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