Design of Protein Functions Using Computational and Experimental Approaches

Research Center of Integrative Molecular Systems
Division of Trans-Hierarchical Molecular Systems

KOSUGI, Takahiro
Assistant Professor

Our research is to design a variety of protein functions using computational and experimental approaches. We try to (1) design enzymes from scratch and reveal the origin of the enzymatic activity, (2) control concerted functions by rationally engineering protein complexes and understand their mechanisms and (3) uncover roles of protein complexes in cells and control cellar functions by creating several customized proteins or protein complexes.

1. Elucidation of Intracellular Functions Using Redesigned Protein Complex

We performed cell biological study based on new approach by rationally engineering protein complexes. Target of Rapamycin (TOR) complex, which is involved in response for their environment and in cell life span, is known to form two types of complexes with different constituent proteins, TORC1 and TORC2. Furthermore, while only one type of TORC1 is in fission yeast and mammals, budding yeast has two types of TORC1, Tor1 and Tor2 derived TORC1. It is known that eliminating only Tor1-TORC1 (deletion of the *tor1* gene) extends cell life span. However, since both TORC1 and TORC2 are essential for yeast and the *tor2* gene cannot be deleted (loss of TORC2), Tor2-TORC1 has never been studied. Nevertheless, Tor1- and Tor2-TORC1 have been thought to play the same role in the cell. Using our protein design technology, we succeeded in creating a modified Tor2 that does not produce only Tor2-TORC1, and revealed that the two TORC1s have different functions.

Reference

1) Y. Kamada, C. Umeda, Y. Mukai, H. Ohtsuka, Y. Otsubo, A. Yamashita and T. Kosugi, *J. Cell Biol.* **137**, jcs261625 (2023).

Award

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