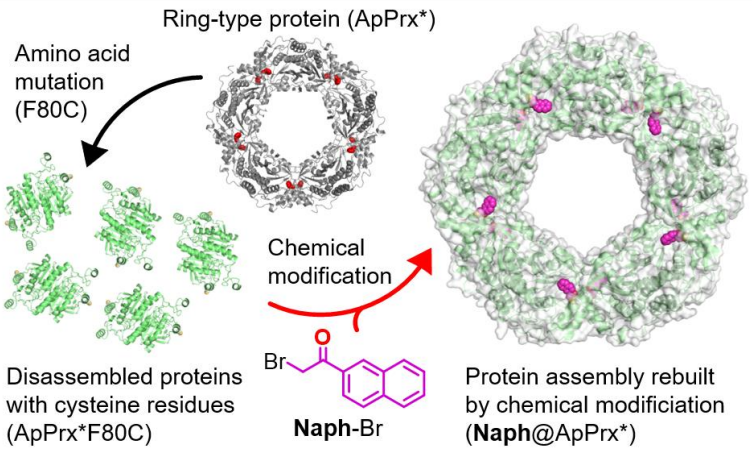
Rebuilding ring-type decameric assembly of peroxiredoxin by chemical modification

(*Biomedical Research Institute, National Institute of Advanced Industrial Science and Technology (AIST)*) ○Tomoki Himiyama, Tsutomu Nakamura
Keywords: Peroxiredoxin; Chemical Modification; Protein Assembly

The quaternary structure (QS) of proteins is generated through specific supramolecular interactions among protein domains, resulting in highly sophisticated architectures such as spheres, tubes, ring-like conformations, and bacterial compartments and viruses.[1] Direct control of protein QS is still challenging owing to the complexity of protein structure. As a protein with a characteristic QS, peroxiredoxin (Prx) is an antioxidant enzyme expressed in most living organisms.[2] It uses cysteine as a catalytic residue and forms characteristic QS including dimers, square octamers, pentagonal decamers, and hexagonal dodecamers. Such structural variations render Prx a noteworthy target for studying protein assembly and its application in nanotechnology. For example, Prx from *Aeropyrum pernix* K1 (ApPrx) forms a characteristic ring-type decamer via the assembly of five dimers.

In this work, we disrupted and reconstituted ApPrx QS via amino acid mutations and chemical modifications targeting hot spots for protein assembly (Figure).[3] Hydrophobic interactions are essential for the ApPrx dimers to associate. The decameric QS of an ApPrx* mutant, wherein all cysteine residues in wild-type ApPrx were mutated to serine, was destructed to dimers via an F80C mutation destructing the hydrophobic interactions. The dimeric ApPrx*F80C mutant was then modified with small molecules and successfully assembled as a decamer by modifying the protein with a naphthalene derivative. Structural analysis confirmed that an artificially installed chemical moiety potentially facilitates suitable protein-protein interactions to rebuild a native structure. This study describes a facile method to regulate protein assembly state.



1) B. J. G. E. Pieters, M. B. van Eldijk, R. J. M. Nolte, J. Mecinović, *Chem. Soc. Rev.* **2016**, *45*, 24. 2) A. Perkins, K. J. Nelson, D. Parsonage, L. B. Poole, P. A. Karplus, *Trends. Biochem. Sci.* **2015**, *40*, 435. 3) a) T. Himiyama, T. Nakamura, *Protein Sci.* **2020**, *29*, 1138. b) T. Himiyama, Y. Tsuchiya, Y. Yonezawa, T. Nakamura, *Bioconjugate Chem.* Article ASAP. doi: 10.1021/acs.bioconjchem.0c00587

© The Chemical Society of Japan