

自己集合中空錯体の孤立空間への捕捉によるタンパク質の安定化

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Protein stabilization by encapsulating into an isolated space of self-assembled hollow cages (¹Graduate School of Engineering, The University of Tokyo, ²Institute for Molecular Science, ³Institute for Integrated Cell-Material Sciences (iCeMS), Kyoto University) ○Risa Ebihara,¹ Takahiro Nakama,¹ Maho Yagi-Utsumi,² Daishi Fujita,³ Makoto Fujita^{1,2}

Encapsulation into an isolated space is of fundamental importance to regulate the structure and function of proteins in biological systems, such as a molecular chaperone that assists protein folding. We have previously reported protein encapsulation into an $M_{12}L_{24}$ hollow spherical complex that forms through the self-assembly of Pd(II) ions (M) and bis(pyridine) ligands (L).^{1,2} Cutinase-like enzyme, CLE was significantly stabilized against heat and organic solvents upon the encapsulation. In this study, to clarify the mechanism of the stability enhancement by confining in the cage, we investigated the enzymatic activity and structure of CLE that was encapsulated in two $M_{12}L_{24}$ complexes of different sizes (Fig. 1). When encapsulated in a larger $M_{12}L_{24}$ cage composed of **L2**, CLE was significantly stabilized and retained its activity in an organic solvent as much as that in the cage of **L1**. ^1H - ^{15}N HSQC NMR shows that the encapsulation in the isolated space of $M_{12}L_{24}$ prevented the protein from aggregation and maintained its active structure.

Keywords : Protein encapsulation; Self-assembly; $M_{12}L_{24}$ cage; Protein stabilization; Nano space

分子シャペロンによるフォールディングの促進をはじめ、タンパク質の孤立空間への閉じ込めは、生体内でその構造や機能を制御する重要な機構である。当研究室では、Pd(II)イオン(M)と配位子(L)の自己組織化により形成する $M_{12}L_{24}$ 中空球状錯体へのタンパク質の包接を報告してきた^(1,2)。 $M_{12}L_{24}$ 錯体へ包接されたクチナーゼ様酵素 CLE は、熱や有機溶媒への耐性が著しく向上した。本研究では、この安定化の機構を解明するため、大きさの異なる 2 種類の $M_{12}L_{24}$ 錯体へ CLE を包接し、その酵素活性・構造を詳細に解析した(Fig. 1)。配位子 **2** (**L2**)を用いて内部空間が拡張された $M_{12}L_{24}$ 錯体内でも、**L1** の場合と同様に CLE は有機溶媒に対する安定性が向上し、酵素活性が保持された。 ^1H - ^{15}N HSQC NMR 測定から、包接した CLE は、中空錯体の孤立空間へ捕捉されることで凝集を抑制され、活性な構造を保持・復元できることが示された。

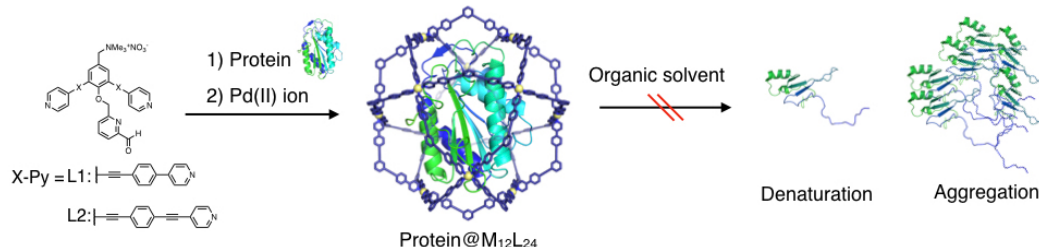


Fig.1 Protein stabilization by encapsulating into $M_{12}L_{24}$ cages of different sizes

1) D. Fujita *et al.*, *Nat. Commun.* **2012**, 3, 1093. 2) D. Fujita, *et al.*, *Chem* **2021**, 7, 2672–2683.