FrenchBIC Webinar

Installing a LPMO-inspired copper binding site onto amyloid-like fibrils

Vincent Lebrun

Equipe Biométaux et Chimie Biologique, Institut de Chimie de Strasbourg (UMR 7177), Université de Strasbourg / CNRS, 4 rue Blaise Pascal, 67000 Strasbourg
vlebrun@unistra.fr

Flexibility of short peptides often impairs their use as ligands for the development of catalytic metal complexes. A way to lock a peptide's conformation is to involve it in a network of intermolecular interactions, such as in amyloid fibrils.[1] The group of Korendovych has demonstrated the potential of such method to develop catalytically active peptide-metal complexes.[2–4]

Lytic Polysaccharide MonoOxygenases (LPMO) are copper enzymes able to oxidatively cleave polysaccharide (eg. cellulose, chitin) that are receiving chemist's attention because of their potential applications.[5]

Here, we describe a "minimalist *de novo* protein design" approach aiming at anchoring a LPMO-inspired copper site onto amyloid-like fibrils. As the copper in LPMO is chelated by two non-equivalent histidines, the design was made in order to preform the metal site via the use of two different peptides, each bringing one histidine. Their sequence was built on those of the "Amyloid Inspired Peptides" developed by the group of Guler.[6]

References

[1] L. R. Marshall, I. V. Korendovych, *Curr. Opin. Chem. Biol.* **2021**, *64*, 145–153.
[2] C. M. Rufo, Y. S. Moroz, O. V. Moroz, J. Stöhr, T. A. Smith, X. Hu, W. F. Degrado, I. V. Korendovych, *Nat. Chem. 2014 64* **2014**, *6*, 303–309.
[3] O. Zozulia, M. A. Dolan, I. V. Korendovych, *Chem. Soc. Rev.* **2018**, *47*, 3621–3639.
[4] L. R. Marshall, O. Zozulia, Z. Lengyel-Zhand, I. V. Korendovych, *ACS Catal.* **2019**, *9*, 9265–9275.
[5] L. Ciano, G. J. Davies, W. B. Tolman, P. H. Walton, *Nat. Catal. 2018 18* **2018**, *1*, 571–577.
[6] G. Cinar, H. Ceylan, M. Urel, T. S. Erkal, E. Deniz Tekin, A. B. Tekinay, A. Dâna, M. O. Guler, *Biomacromolecules* **2012**, *13*, 3377–3387.