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Protein-polymer conjugates as a new type of artificial enzymes

AUTHORS
Changzhu WU / UNIVERSITY OF SOUTHERN DENMARK, CAMPUSVEJ 55, ODENSE

PURPOSE OF THE ABSTRACT

Artificial enzymes, usually created by incorporating one or two abiological catalytic species into protein hosts, are becoming promising tools for biocatalysis. However, they are still far behind natural enzymes due to their limited active sites with low activity and selectivity.

Here, I present a new approach to preparing artificial enzymes by combining proteins with catalytically active polymers, generating so-called ?artificial polyenzymes? (ArPoly), see Figure 1. Different from traditional artificial enzymes, ArPoly can be easily tailored for their structure, composition, catalysis loading, and active sites. This tunability allows ArPoly to carry out the catalysis with not only high reactivity but also new-to-nature selectivity.

Our first proof-of-concept study is to combine protein scaffolds with proline polymers using the atom transfer radical polymerization (ATRP) method to graft polymer from proteins.[1] Surprisingly, the resultant ArPoly is highly water-soluble, allowing for the asymmetric aldol reaction in pure water, which is the first report for water-soluble proline catalysts. Our study further suggests that this new-to-nature reactivity is due to the synergetic effects between proline catalysts and protein scaffolds.

Taking advantage of high controllability, the polymer structure on ArPoly can be tailored. In this context, polystyrene and polyproline are copolymerized from the protein surface with their composition finely adjusted.[2] Since the hydrophobic microenvironment promotes proline-catalyzed aldol reactions, the tailored ArPoly containing polystyrene contributes to remarkable catalytic efficiency and selectivity (i.e., 94% conversion and 98% ee), which is a significant improvement compared to the prototype ArPoly.

In addition to catalytic polymers, active ligands are polymerized to protein, thereafter, coordinated with metal ions, generating metal-containing artificial polyenzymes. To demonstrate this possibility, ArPoly is conjugated with proline polymers that are in situ coordinated with Cu (II) to form a metal complex during the ARTP preparation.[3] The resulting ArPoly is then used as a clickase for highly efficient click reactions. Importantly, the artificial clickase is biocompatible, causing no cytotoxicity cells, thus becoming promising catalysts for bioorthogonal chemistry. Moreover, we further expand our toolbox by polymerizing chiral ligands from proteins and then coordinating with Ru metal.[4] We demonstrate that the metal-containing ArPoly allows for asymmetric hydrogenation with almost 100% yield and 93% ee. More interestingly, the metal-containing polymer can be grafted from transaminase, which enables the enzyme to transform amine to chiral alcohol, creating the new-to-nature reactivity that the parental enzyme doesn't have.

To summarize, my group is dedicated to developing artificial polyenzymes (ArPoly) for catalysis by combining active polymers with proteins/enzymes. We have showcased four different types of ArPoly, in which polymer active units, structures, and compositions are tailored to enable not only high activity and selectivity but also new-to-nature reactions.

FIGURES

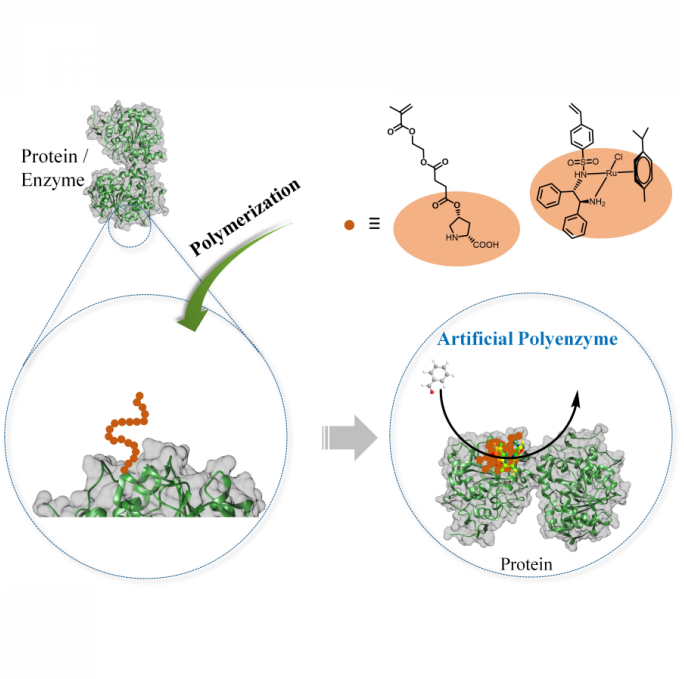

FIGURE 1

Figure 1

Artificial polyenzymes (ArPoly) combining proteins and polymers

FIGURE 2

KEYWORDS

Artificial enzyme | Artificial polyenzyme | polymer-protein conjugate | Asymmetric reaction

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