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Dinucleotide-based artificial cofactors: preparation and applications in photobiocatalysis

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PURPOSE OF THE ABSTRACT
Nature has generated an impressive array of chemical reactivities in enzymes using only a subset of the 20 proteinogenic amino acids. However, this chemistry is mostly limited to general acid-base catalysis, nucleophilic and electrophilic catalysis. To expand on the chemical reactivities, nature employs cofactors, which are utilised in roughly half of all reactions catalysed by enzymes. Those cofactors can be divided into inorganic, metal-organic, and organic cofactors. The drive to create new-to-nature functions for biocatalysis requires the expansion or modulation of the natural sets of amino acids and cofactors.

New-to-nature functions have been implemented by the incorporation of non-canonical amino acids (ncAAs), bioconjugation or supramolecular assembly approaches of cofactors and catalysts. Artificial metalloenzymes are one of the prominent examples. However, artificial organic cofactors have yet seen less attention.

Photocatalysis has gained increasing attention to promote otherwise inaccessible reactions by organic synthesis. Photocatalytic reactions often lack stereo- and/or enantioselective control. To overcome this limitation the combination of photocatalysts with the chiral environment of a protein is particularly promising. To date, most photocatalytic approaches have been realised by integrating inorganic or metal-organic photocatalysts either in enzymatic cascade reactions or as cofactors in artificial metalloenzymes. Since these photocatalysts are often based on transition metals, organic photocatalysts could serve as a sustainable alternative.

Photobiocatalysis using organic photocatalysts is still underrepresented with only few known examples. We envision to install novel moieties onto known cofactors. Therefore, we have harnessed the base exchange activity of ADP-ribosyl cyclase from Aplysia californica to covalently link organic photocatalytsts to an ADP-ribose backbone. This furnishes an artificial photocatalytic dinucleotide-like cofactor. We aim to utilize the binding characteristics of dinucleotide cofactors, which are mediated to a large extend by the adenosine ring and the phosphodiester group. This allows us to implement a dinucleotide-like cofactor with novel reactivities in given protein scaffolds. This seems particularly promising as many well-known biocatalysts with desirable properties bind dinucleotides. Our setup also allows for easy and direct access of artificial dinucleotide cofactors with modified or improved characteristics not limited to photobiocatalysis. We are currently working on optimizing the performance of the cyclase to establish a versatile tool for the generation of artificial dinucleotide-like cofactors.

FIGURES

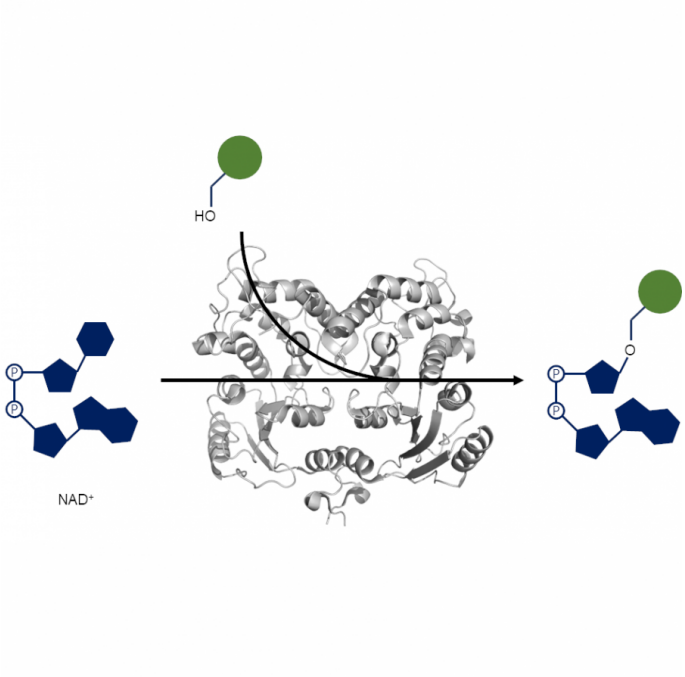

FIGURE 1

Artificial dinucleotide cofactors by enzymatic reaction

General concept of ADPRC-catalysed base exchange reaction with photocatalysts to generate artificial photocatalytic dinculeotide cofactors

FIGURE 2

KEYWORDS

Artificial cofactors | Photobiocatalysis | New-to-nature functionalities | Protein engineering

BIBLIOGRAPHY