BIOTRANS
LA ROCHELLE 2023

N°1486 / PC
TOPIC(s) : Artificial enzymes and de-novo enzyme design

Lights on and action: De novo metalloproteins for photocatalytic diol cleavage

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PURPOSE OF THE ABSTRACT

Enzymes are efficient biocatalysts coupled with tremendous chemo-, regio- and stereoselectivity. Nevertheless, their reaction repertoire is usually confined to the natural chemical space. A large variety of reactions known in organic chemistry therefore remain inaccessible, limiting the applications of these sustainable biocatalysts. With the ongoing advancement of computational methods in the field of protein design, it is now possible to generate desired protein scaffolds de novo and equip them with new catalytic functions.[1–3]

Here we demonstrate the development of a photoenzyme based on a de novo protein equipped with a metal-binding site that selectively and with high affinity binds lanthanide ions, such as cerium(III) (A).[4] By irradiation with visible light, this artificial metalloprotein is able to photocatalytically cleave the C–C bond of vicinal diols via a radical mechanism and thus extends the reaction space of natural enzymes by a new-to-nature reaction (B).

The enzyme was improved by site saturation mutagenesis and consecutive rational design of the active site. The result of these initial screenings is a variant with higher photostability, faster lanthanide binding kinetics, and improved yield for the C–C bond cleavage of the model substrate hydrobenzoin and derivatives thereof, converting it into the corresponding carbonyl compounds. Future investigations will focus on the stereoselectivity of chiral substrates.

FIGURES

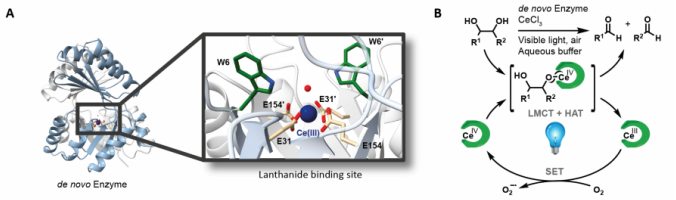

FIGURE 1

Photocatalytic cleavage of vicinal diols by a de novo metalloprotein

A) Cerium (III) bound to the active site of the de novo metalloprotein. B) Proposed radical mechanism for the photocatalytic cleavage of vicinal diols.

FIGURE 2

KEYWORDS

de novo metalloprotein | photocatalysis | C-C bond cleavage | cerium(III) catalysis

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