Engineered Metalloenzymes for Stereocontrolled Atom Transfer Radical Addition

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BACKGROUND

Over the past three decades, the advent of directed evolution has enabled enhancements to catalytic activity and stereoselectivity through customized enzymes; demonstrating the potential of biocatalysis to revolutionize the practice of asymmetric synthesis. Until recently, however, the catalytic repertoire of enzymes has been mostly limited to reactions found in nature, posing constraints on the types of products available from enzyme catalysis. Furthermore, to date, a variety of catalysis modes discovered and optimized by synthetic chemists has remained out of reach of natural enzymes. It follows that bringing new catalytic functions to naturally-occurring enzymes can dramatically expand the repertoire of enzymology and generate novel biocatalysts applicable to fields such as pharmaceuticals and agrochemistry.

DESCRIPTION

Researchers at the University of California, Santa Barbara have repurposed naturally occurring metalloenzymes to catalyze unnatural radical reactions in a stereocontrolled fashion. Steering the absolute and relative stereochemistry of these free radical processes is notoriously difficult in asymmetric catalysis, however, this technology imposes excellent stereocontrol over the radical addition step and the halogen rebound step, allowing enantio- and diastereodivergent radical catalysis to be easily carried out. These metalloenzymes are fully genetically encoded, highly active at room temperature (up to 20,000 total turnover number), and readily function in bacterial cells and cell-free lysates. This evolvable metalloenzyme platform represents a promising solution to tame fleeting radical intermediates for asymmetric catalysis.

ADVANTAGES

- Solves the difficulty of imposing enantio- and diastereocontrol over free radical-mediated bond forming processes
- Highly active at room temperature
- Fully genetically encoded and ready to function in bacterial cells and cell-free lysates
- Enables efficient preparation of chiral small-molecule agents

APPLICATIONS

- Pharmaceuticals and biotechnology

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OTHER INFORMATION

KEYWORDS

stereochemistry, biocatalysis, stereoselectivity, enzymes, pharmaceuticals, agrochemistry, metalloenzymes, asymmetric catalysis, diastereocontrol, enantiocontrol, free radical-mediated, genetic, bacterial cell, chiral

CATEGORIZED AS

- **Agriculture & Animal Science**
  - Chemicals
  - Plant Varieties
- **Biotechnology**
  - Bioinformatics
  - Health
  - Other
  - Proteomics

RELATED CASES

2021-975-0

- Biomolecular science
- Agriculture

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	20240336943	10/10/2024	2021-975

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Compositions, Systems, and Methods for Stereoselective Synthesis of Non-Canonical Amino Acids
- Compositions, Systems, and Methods for Stereoselective Decarboxylative Radical Cyclization
- Advanced Biocatalytic Methods for the Synthesis of Non-Canonical Amino Acids and Amine Derivatives
- Systems, Compositions And Methods Of Metalloprotein-Catalyzed Fluorination, Azidation, Thiocyanation and Hydroxylation
- Enzyme-Controlled Stereoselective Radical Cyclisation to Arenes Enabled by Metalloredox Biocatalysis

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