



**Systems, Compositions And Methods Of Metalloprotein-Catalyzed Fluorination, Azidation, Thiocyanation and Hydroxylation**

Tech ID: 33416 / UC Case 2024-841-0

**CONTACT**

Donna M. Cyr  
[cyr@tia.ucsb.edu](mailto:cyr@tia.ucsb.edu)  
tel: .

**INVENTORS**

- ▶ Guo, Rui
- ▶ Yang, Yang
- ▶ Zhao, Liu-Peng

**OTHER INFORMATION**

**KEYWORDS**

biochemical, biocatalysis,  
  
enzymes, fluorine,  
  
pharmaceuticals,  
  
agrochemicals, synthetic  
  
chemistry

**CATEGORIZED AS**

- ▶ **Biotechnology**
- ▶ Health
- ▶ Other

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2024-841-0

BACKGROUND

Over the past decade, groundbreaking studies on unnatural biocatalysis have transformed the biochemical landscape of natural enzymes to encompass biocatalytic reactions that have not previously been encountered in nature. Drawing inspiration from synthetic, organic, and organometallic chemistry, biocatalysis researchers have developed a range of novel nonnatural enzymatic activities. Together, these efforts substantially expanded the reaction capabilities of enzyme catalysis and furnished powerful tools for chemical synthesis. Despite these notable advances, nonnatural enzymatic processes for C-F bond formation have long eluded the biocatalysis community. The incorporation of fluorine into organic compounds can lead to enhanced bioavailability, metabolic stability, and desirable protein binding profiles. Due to the central importance of organofluorine compounds in the pharmaceutical and agrochemical industries, fluorine biocatalysis and synthetic biology has been a long-standing challenge. Additionally, it is beneficial to streamline the synthesis of molecular architecture, and it is desirable to provide enzymes and methods for C-H functionalization, in the presence of fluorine or exogenous anions, to access valuable organic compounds such as organofluorine compounds.

DESCRIPTION

Researchers at the University of California, Santa Barbara have repurposed and evolved nonheme iron (Fe) enzymes to promote new-to-nature C-H fluorination reactions with excellent efficiency. These evolved Fe enzymes represent the first synthetic fluorinases capable of catalyzing the formation of C-F bonds. The newly engineered Fe-dependent fluorinases complement the naturally occurring fluorinase activity found only in bacteria and archaea by exploiting an underutilized radical mechanism for enzymatic C-F bond formation. The directed evolution of nonheme Fe enzymes affords valuable tools for the biocatalytic synthesis of organofluorine compounds via a C-H functionalization logic. Further development and optimization of this technology has the potential to be applied in the biocatalytic synthesis of fluorine-containing drug small molecules or their intermediates.

ADVANTAGES

- ▶ Promotes new-to-nature C-H fluorination reactions with excellent efficiency
- ▶ Affords valuable tools for the biocatalytic synthesis of organofluorine compounds
- ▶ Has the potential to be applied in the biocatalytic synthesis of fluorine-containing drug small molecules

APPLICATIONS

- ▶ Pharmaceuticals
- ▶ Agrochemicals

PATENT STATUS

Country	Type	Number	Dated	Case
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Additional Patent Pending

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](#)
- [Engineered Metalloenzymes for Stereocontrolled Atom Transfer Radical Addition](#)
- [Enzyme-Controlled Stereoselective Radical Cyclisation to Arenes Enabled by Metalloredux Biocatalysis](#)

University of California, Santa Barbara  
Office of Technology & Industry Alliances  
342 Lagoon Road, ,Santa Barbara,CA 93106-2055 |  
<https://www.tia.ucsb.edu>  
Tel: 805-893-2073 | Fax: 805.893.5236 | [padilla@tia.ucsb.edu](mailto:padilla@tia.ucsb.edu)



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