Compositions, Systems, and Methods for Stereoselective Synthesis of Non-Canonical Amino Acids

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BACKGROUND

Biocatalysis is a promising mode of realizing previously inaccessible chemical reactions while imposing exquisite stereocontrol over the synthesis. Insights from synthetic chemistry and small molecule catalysis have enabled researchers to repurpose and evolve natural metalloenzymes, and flavin- and nicotinamide-dependent enzymes to catalyze stereoselective nonnatural reactions as well as processes mediated by carbon- and nitrogen-centered radicals. Collectively, these efforts significantly expanded the catalytic repertoire of enzymes that encompass synthetically valuable reactions not previously known in biology that can be applied to high-priority topics such as therapeutics and sustainable energy production. Despite these advances, it is essential to further develop general and synthetically-useful enzymatic activation modes that are both new-to-chemistry and new-to-biology.

DESCRIPTION

Researchers at the University of California, Santa Barbara (UCSB) have enabled highly stereoselective synthesis of diverse and valuable non-canonical amino acids by synergistically combining engineering photoredox and pyridoxal phosphate enzymes to create a biologically and chemically novel activation mode. The non-canonical amino acids produced by this novel methodology include those bearing challenging stereochemical dyads and triads, prepared in a convergent and protecting-group-free fashion with excellent diastereo- and enantiocontrol. Notably, the a-stereochemistry of the non-canonical amino acids can be edited, giving rise to either the natural L-amino acids or the unnatural D-amino acids with excellent enantioselectivity. The combined enzyme engineering and synergetic photoredox and pyridoxal radical biocatalysis created by the UCSB researchers represents a powerful platform to discover new catalytic reactions and to tame free radical intermediates for asymmetric catalysis.

ADVANTAGES

- Allows diverse and valuable non-canonical amino acids to be prepared with excellent enantio- and diastereoselectivity
- New-to-nature and new-to-chemistry activation mode presents a powerful platform for further discovery

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OTHER INFORMATION

KEYWORDS

biocatalysis, synthetic chemistry, enzymes, amino acids

CATEGORIZED AS

- **Biotechnology**
  - Health

RELATED CASES

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APPLICATIONS

- Peptide therapeutics
- Bioactive natural products
- Biomedically-useful functional nonnatural proteins

PATENT STATUS

Patent Pending

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Compositions, Systems, and Methods for Stereoselective Decarboxylative Radical Cyclization
- Engineered Metalloenzymes for Stereocontrolled Atom Transfer Radical Addition
- 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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