LIGHT-DRIVEN KINETIC RESOLUTION OF A-FUNCTIONALIZED ACIDS ENABLED BY ENGINEERED FATTY ACID PHOTODECARBOXYLASE

Danyang Li, Zhejiang University, China
lidanyangde@foxmail.com
Jian Xu, Zhejiang University, China
Xianfu Lin, Zhejiang University, China
Qi Wu, Zhejiang University, China

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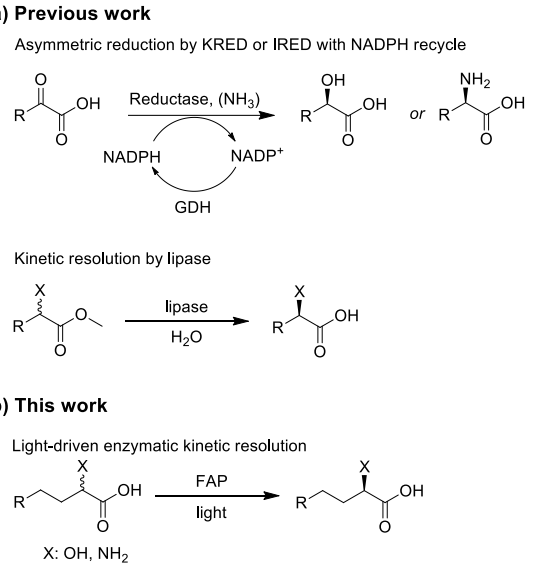
Multifunctional chiral molecules such as unnatural α-amino acids and α-hydroxy acids are valuable precursors to a variety of medicines and natural products.[1] The biocatalysis provides a greener and more sustainable process than transition metal catalysts and complex chiral ligands. For example, keto reductases (KRED) and imine reductases (IRED) have been successfully used to convert α-keto acids into α-hydroxy/amino acids.[2] Another widely used method was kinetic resolution (KR) or dynamic kinetic resolution (DKR) by employing lipases.[3] Herein, we described the variants of fatty acid photodecarboxylase (C*v*FAP), which was used to convert long-chain fatty acids into hydrocarbons,[4] catalyze kinetic resolution of α-amino acids and α-hydroxy acids with high conversion and excellent nonreacted (*R*)-configured substrate stereoselectivity (ee up to 99%). This efficient light-driven process does not require NADPH recycle nor prerequisite preparation of esters in contrast with other biocatalytic methods (Scheme 1). To our delight, although most biocatalysts are hardly to be universal, the best mutant G462Y displayed a satisfactory substrate scope (Figure 1). The structure-guided engineering strategy was introduced by large-size amino acid scanning at hot position to narrow the substrate binding tunnel. We believed that this research conformed to the conference topic of Enzyme promiscuity, evolution and dynamics.



Scheme 1. Enzymatic asymmetric synthesis of α-hydroxy/amino acids

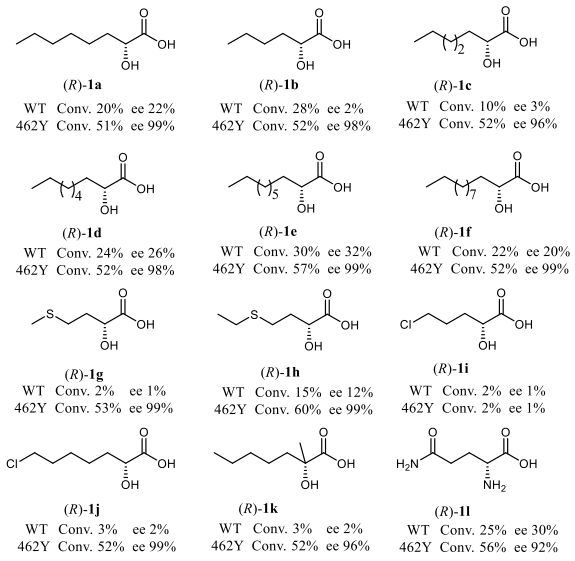


Figure 1. Substrate scope of light-driven kinetic resolution enabled by WT CvFAP and variant G462Y

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