Photoinduced Imine Reductions Catalyzed by an Artificial Photoredox Enzyme Containing a Photosensitizer with a Protein Matrix

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Imine reduction is an important reaction for generating useful bioactive amines. Various catalysts have been reported to promote this reaction, with photoredox catalysts emerging as promising candidates for sustainable amine synthesis. Developing this reaction using biomolecules as scaffolds is expected to expand its utility.[1] Previously, a unique cyclic reaction network has been constructed to achieve enantioselective imine reductions using a combination of a photoredox catalyst and a natural enzyme.[2] However, the integration of photoredox catalysts with biomolecules has been limited. In this context, we have recently investigated the incorporation of a xanthene dye into a protein matrix as an artificial photoredox enzyme for the photoreduction of dihydroisoquinoline derivatives (Fig. 1).

In this study, fluorescein or eosin Y was employed as an organic photosensitizer, and lipocalin, a protein previously engineered to bind a fluorescein molecule for living cell imaging, was employed.[3] First, computational optimization of protein sequence yielded a variant with a 7-fold increase in expression yield. Second, mutations around the dye-binding site of the protein matrix were performed to improve the catalytic activities for photoinduced imine reductions. Site-directed mutations of potent residues suggested by alanine scanning were carried out. Fluorescein in the H86D mutant exhibited 3.5-fold higher catalytic activity compared to that from the wild-type protein. Fluorescence titration of the substrate revealed that the high binding affinity of the substrate for the H86D mutant incorporating the xanthene dye contributed to the improvement in the catalytic ability.

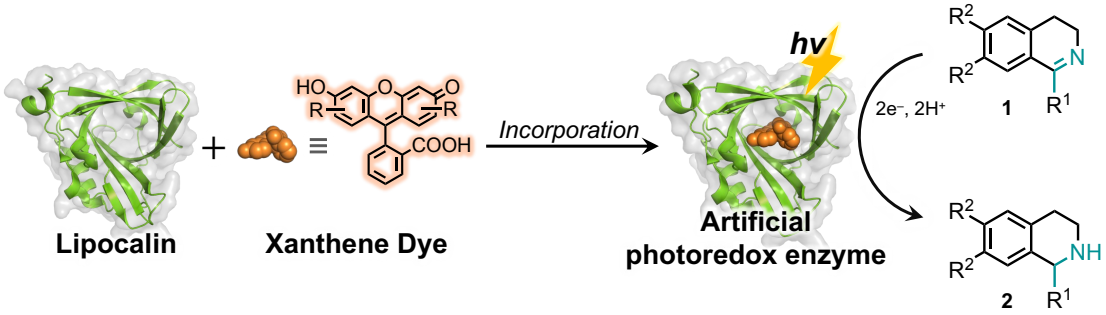

Fig. 1. Photoinduced imine reduction catalyzed by an artificial photoredox enzyme.

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