Bridging Between Organocatalysis and Biocatalysis: The Powerful Enamine Mechanism of Organocatalysts Engineered into the Tautomerase Superfamily Scaffold

Fact Sheet

Project information

PROZYMES
Grant agreement ID: 242293
Status
Closed project

Funded under:
FP7-IDEAS-ERC
Overall budget:
€ 2 000 000

EU contribution
€ 2 000 000

Hosted by:
RIJKSUNIVERSITEIT GRONINGEN
Netherlands

Objective

Proline and related secondary amines were found to be efficient organocatalysts of aldol, alkylation, Michael addition, and other challenging bond-forming reactions. The design of even more efficient systems that would allow extending this remarkable catalytic strategy to a useful and environmentally benign synthetic methodology would be highly desirable. This proposal aims to develop a new class of biocatalysts that use the powerful proline-based enamine mechanism of organocatalysts but that take advantage of the water solubility and stereochemical control available with enzymes. As a scaffold for engineering, we will exploit the active-site template of the tautomerase superfamily proteins, the only known group of enzymes that has the unique feature of using a N-terminal proline in catalysis. By systematically screening tautomerasers for promiscuous carbonyl transformation activities, we aim to demonstrate that Pro-1 residues within these tautomerasers can react with carbonyl compounds to give enamine intermediates, and thus may facilitate various bond-forming reactions. The most promising enzymes will be used in directed evolution experiments to enhance the desired activities to a practical level. For this, new screening and selection methods will be developed that allow the efficient passage through protein sequence space. Furthermore, unnatural secondary amines will be introduced by total chemical synthesis. In this way, we envision to generate superior biocatalysts for carbon-carbon bond-forming reactions. The idea of using a protein scaffold in which a catalytic proline is present as nucleophile and that has a unique
reactivity to form enamines would be a completely new approach to making carbon-carbon bonds. It does not copy something in Nature, but is based on the synthetic requirements of the desired bond-forming reactions. I believe that this type of approach is the future of enzyme engineering and is the key to more application of biocatalysis in industry.

Field of Science
/engineering and technology/industrial biotechnology/bioprocessing technologies/biocatalysis

Programme(s)
FP7-IDEAS-ERC - Specific programme: "Ideas" implementing the Seventh Framework Programme of the European Community for research, technological development and demonstration activities (2007 to 2013)

Topic(s)
ERC-SG-LS9 - ERC Starting Grant - Applied life sciences and biotechnology

Call for proposal
ERC-2009-StG
See other projects for this call

Funding Scheme
ERC-SG - ERC Starting Grant

Principal Investigator
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Host institution
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Activity type
Higher or Secondary
Education Establishments

EU Contribution
€ 2 000 000

Website
Contact the organisation

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Beneficiaries (1)

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