EngBiocat

Implementing an Enzyme Engineering Technology Platform for the provision of tailor-made enzymes for biocatalytic processes

The project addressed the development of a technology platform for the fast and efficient implementation of biocatalytic processes. Within the project we established a biocatalytic toolbox for new and innovative synthetic routes to the chiral amines that are of main industrial interest. The consortium consisted of 9 partners from 5 countries, including DSM as an industrial partner, 3 SMEs and 5 academic institutions. The partner structure enabled an interdisciplinary approach covering all aspects from the enzyme to the final product molecule.

Current drawbacks in the application of biocatalysis for chiral amine synthesis are the limited substrate scope of the enzymes and the inefficient synthetic processes. The main technology used in this project to overcome these limitations was enzyme engineering, which was combined with efficient enzyme production systems and the optimization of the synthetic process. By the application of model-based enzyme variant library design and efficient screening technologies, we were able to achieve major breakthroughs in the adaptation of the enzymes to the synthetic processes. For two enzyme classes – transaminases and lyases – we developed enzyme variants that are able to synthesize a broader variety of chiral amines, which are not accessible through the use of the wild-type enzymes. The main hurdle in the application of transaminases in a preparative synthetic reaction is the inefficient transformation at a high substrate concentration and the problem of equilibrium considerations. Although the equilibrium cannot be changed by enzyme optimization, theoretical calculations within the consortium guided the process design, which subsequently led to the development of improved enzyme variants under the project conditions. It was possible to immobilize the biocatalyst with full retention of activity, so that it could be used several times over in the synthetic process, which allows a drastic reduction of the synthetic costs. Overall, the consortium developed a biocatalyst platform that covers the whole chain, from biocatalyst optimization through biocatalyst production to biocatalyst immobilization, as well as discovering an efficient synthesis process for chiral amines.

Partners involved in the EngBiocat project

Project coordinator

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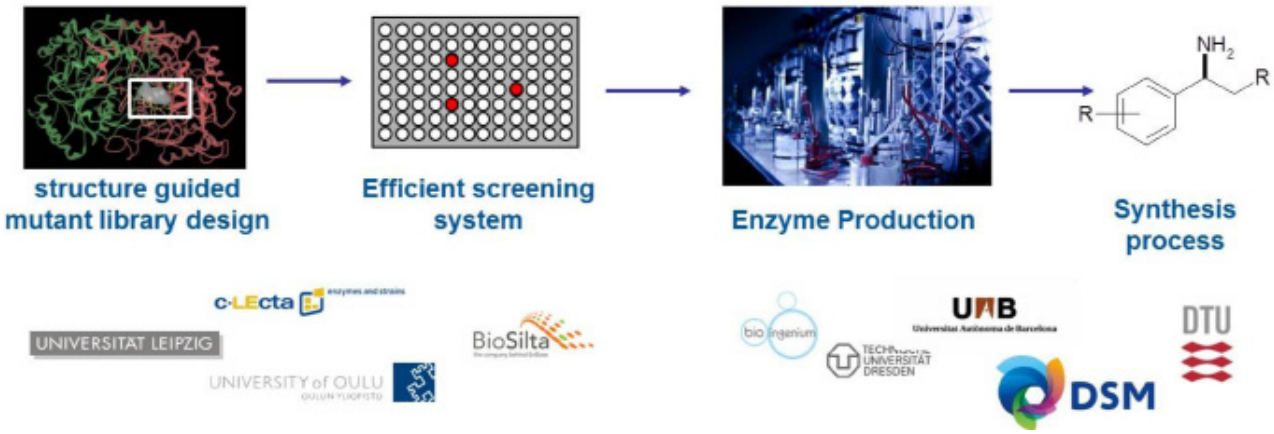
Within the joint research project "Eng Biocat" the consortium partners aim to develop and implement a fully ***integrated enzyme engineering platform which can be used to rapidly identify new enzyme mutants which allow the biosynthesis of novel chemicals products with high industrial relevance.*** The consortium is made up by three SMEs (c-LEcta, Biosilta, Bioingenium), one industry partner (DSM Pharmaceutical Products) and 5 academic institutions (Technical University of Denmark, Prof. Woodley; Technical University of Dresden, Prof. Barth; University of Oulu, Dr. Hillukkala; Universitat Autònoma de Barcelona, Prof. López-Santín; University of Leipzig, Prof. Hofmann). The consortium is coordinated by the German biotechnology company c-LEcta.



c-LEcta GmbH is specialized in the discovery, optimization and production of enzymes and in strain engineering techniques for protein and small molecule production.

During enzyme discovery projects c-LEcta screens genomic, microbial and metagenomic libraries that have been assembled from natural microbial diversity. A range of proprietary expression hosts are available (E. coli, Bacillus, Pichia), complete with the full range of molecular tools. During its enzyme optimization projects, c-LEcta employs its proprietary 'cluster screening' for the efficient identification of improved enzymes.

This approach is based on 96 well plates and is highly flexible, fast and cost-effective. In order to optimize enzyme function and properties, c-LEcta has developed expertise in directed evolution by mutagenesis, recombination methods and 3D-structure modelling.