Harnessing Nature: Biocatalysis for Industrial Applications

Rebecca Buller

Competence Center for Biocatalysis, Institute for Chemistry and Biotechnology,
Zurich University of Applied Sciences, Einsiedlerstrasse 31, 8820 Wädenswil, Switzerland

rebecca.buller@zhaw.ch

Industrial biocatalysis has developed at a rapid pace and today the use of enzymatic catalysts is more frequently considered in chemical process design. However, in the development race between synthetic chemistry and biocatalysis the latter is still at a disadvantage. Synthetic organic expertise is still much more ingrained in almost all chemical companies, and synthetic catalyst systems are more prevalent in an off-the-shelf format than their enzymatic counterparts. As a consequence, fast development of a biocatalytic process step is more likely if a suitable enzyme is already available (1).

To meet this demand and expand the biocatalytic toolbox, we looked into identifying new members of the synthetically promising ene reductases enzyme family, oxidoreductases, which catalyze the asymmetric reduction of double bonds. We screened 19 bacterial strains for double bond reduction activity using the model substrates cyclohexanone and carvone. Overall, we identified 47 genes coding for putative ene reductases. Remarkably, bioinformatic analysis of all genes and the biochemical characterization of four representative novel ene reductases led us to propose the existence of two new Old Yellow Enzyme subclasses, which we named OYE class III and class IV. By analyzing the substrate scope of the newly discovered biocatalysts and carrying out preparative reactions, we show the potential of these enzymes for future industrial use (2).

The second part of the lecture will highlight our efforts to engineer enzymes for synthetically highly interesting chemistries such as regio- and stereoselective CH activation. Here, we set out to optimize a halogenase for the regio-and enantioselective chlorination of a small molecule of pharmaceutical interest (3). Using a rational enzyme design approach, we show that the enzymatic halogenation method provides new opportunities to overcome the hurdles imposed by purely chemical approaches. The biochemical characterization of the (novel) enzymes further showcases their application potential.

(1) R. Buller, K. Hecht, M. Mirata and H.-P. Meyer in Biocatalysis: An Industrial Perspective (Eds Gonzalo de Gonzalo, Pablo Dominguez de Maria), Royal Society of Chemistry, p.1-43 (2017)
(2) C. Peters, D. Frasson, M. Sievers and R. Buller, *ChemBioChem*, **20 (12)**, 1569-1577 (2019).
(3) T. Hayashi, M. Ligibel, E. Sager, M. Voss, J. Hunziker, K. Schroer, R. Snajdrova and R. Buller, submitted.