

Editorial

Recent Advances on Biocatalysis and Metabolic Engineering for Biomanufacturing

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The use of biocatalysts, including enzymes and metabolically engineered cells, has attracted a great deal of attention in chemical and bio-industry, because biocatalytic reactions can be conducted under environmentally-benign conditions and in more sustainable ways. The catalytic efficiency and chemo-, regio-, and stereo-selectivity of enzymes can be enhanced and modulated using protein engineering. Metabolic engineering seeks to enhance cellular biosynthetic productivity of target metabolites via controlling and redesigning metabolic pathways using multi-omics analysis, genome-scale modeling, metabolic flux control, and reconstruction of novel pathways.

The aim of this Special Issue was to deal with the recent advances in biocatalysis and metabolic engineering for biomanufacturing of biofuels, chemicals, biomaterials, and pharmaceuticals. Reviews and original research articles on the development of new strategies to improve the catalytic efficiency of enzyme, biosynthetic capability of cell factory, and their applications in production of various bioproducts and chemicals have been published.

This special issue on “Recent Advances on Biocatalysis and Metabolic Engineering for Biomanufacturing” includes 18 published articles including review and original research papers. Among the research articles presented in this issue, there is a set of studies on enzyme catalysis, which was a powerful tool to effectively synthesize various target products. In more detail, Mulay et al. investigated *Candida antarctica* Lipase B-catalyzed transesterification of methyl 3-mercaptopropionate with tetraethylene glycol (TEG) and poly(ethylene glycol)s (PEG)s to synthesize thiol-functionalized TEGs and TEGs without use of solvent [1]. Joo et al. reported the biosynthesis of ω -hydroxydodecanoic acid via whole-cell biotransformations using a novel monooxygenase CYP153AL.m from *Limnobacter* sp. 105 MED [2]. ω -Aminododecanoic acid can be used as Nylon 12 monomers. The biotransformation of dodecanoic acid to ω -aminododecanoic acid has been achieved by using an artificial self-sufficient P450, ω -transaminase, and alcohol dehydrogenase, as reported by Ahsan et al. [3].

This issue also covers several studies concerning the characterization of novel enzymes that become more attractive biocatalysts to serve as an alternative platform for chemical synthesis. Senger et al. successfully analyzed the infrared characterization of [NiFe]-hydrogenase from *Escherichia coli* HYD-2 by in situ attenuated total reflection Fourier-transform infrared spectroscopy which proved as an efficient and powerful technique for the analysis of biological macromolecules and enzymatic small molecule catalysis [4]. Glyoxal oxidase, an extracellular oxidoreductase that oxidizes aldehydes and α -hydroxy carbonyl substrates coupled to the reduction of O_2 to H_2O_2 , from *Myceliophthora thermophyla*, has been characterized by Kadowaki et al. [5]. In addition, hydroxylation mechanism of soluble methane monooxygenase from *Methylosinus sporium* strain 5, a type II methanotrophs, was reported by Park et al., which revealed that two molar equivalents of methane monooxygenase regulatory protein B (MMOB) are necessary to achieve catalytic activities toward a broad range of substrates including alkanes, alkenes, halogens, and aromatics [6].

Several investigations in this issue focused on the development of immobilization methods for better biocatalytic performance. By using mannose-functionalized magnetic nanoparticles, Li et al. successfully immobilized *E. coli* cells harboring recombinant glycerol dehydrogenase gene, which showed two-fold higher production of 1,3-dihydroxyacetone from glycerol, compared to the free cells [7]. An optimized procedure of fluorescein diacetate hydrolysis for quantifying total enzymatic activity in the whole biofilm on the carrier without disturbing immobilization was reported by Dzionek et al., which can serve as a promising method to evaluate the physiological state of immobilized bacterial cells [8]. Additionally, Arana-Peña et al. reported the immobilization of Eversa lipase on octyl and aminated agarose beads for the first time, which greatly enhanced the stability of the enzyme [9]. The immobilized enzymes prepared by the cross-linked enzyme aggregates (CLEA) have become more attractive due to their simple preparation and high catalytic efficiency. In this issue, the magnetic cross-linked aggregates of amyloglucosidase was successfully achieved by Amaral-Fonseca et al. [10]. Especially the conditions or factors for the preparation of combi-CLEAs, such as the proportion of enzymes, the type of cross-linker, and coupling temperature, were intensively reviewed by Xu et al. [11].

The last part of this special issue focuses on metabolic engineering of various microorganism for the production of value-added products. Kim et al. reported the enhancement of (-)- α -bisabolol productivity by creating a more efficient heterologous mevalonate pathway [12]. An engineered *E. coli* strain for the conversion of acetate to 3-hydroxypropionic acid by heterologous expression of malonyl-CoA reductase from *Chloroflexus aurantiacus* and the activation of acetate assimilating pathway and glyoxylate shunt pathway was developed by Lee et al. [13]. Baritugo et al. developed a novel tunable promoter system based on repeats of the *Vitreoscilla* hemoglobin promoter and subsequently used for 5-aminovaleric acid and gamma-aminobutyric acid production in several *C. glutamicum* strains [14]. Three intensive reviews on various aspects on metabolic engineering have been published in this issue. Xie et al. highlighted insights into the current advances of monoterpene bioproduction and future outlook to promote the industrial production of valuable monoterpenes [15]. Recent advances in synthetic biology are greatly useful for achieving metabolic engineering purposes, which have been intensively reviewed by Lee et al. [16]. The technological gaps and effective approaches for process intensification of bio-hydrogen production were reviewed by Sun et al., particularly on the latest methods of chemicals/metal addition for improving hydrogen generation during dark fermentation processes [17]. Furthermore, this special issue includes the investigation on mass transfer performance of a novel string film reactor for the aerobic conversion of methane gas, investigated by Mariyana et al., to address process intensification issue on biomanufacturing [18].

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References

1. Mulay, P.; Shrikhande, G.; Puskas, J.E. Synthesis of Mono- and Dithiols of Tetraethylene Glycol and Poly(ethylene glycol)s via Enzyme Catalysis. *Catalysts* **2019**, *9*, 228. [[CrossRef](#)]
2. Joo, S.-Y.; Yoo, H.-W.; Sarak, S.; Kim, B.-G.; Yun, H. Enzymatic Synthesis of ω -Hydroxydodecanoic Acid By Employing a Cytochrome P450 from *Limnobacter* sp. 105 MED. *Catalysts* **2019**, *9*, 54. [[CrossRef](#)]
3. Ahsan, M.M.; Patil, M.D.; Jeon, H.; Sung, S.; Chung, T.; Yun, H. Biosynthesis of Nylon 12 Monomer, ω -Aminododecanoic Acid Using Artificial Self-Sufficient P450, AlkJ and ω -TA. *Catalysts* **2018**, *8*, 400. [[CrossRef](#)]
4. Senger, M.; Laun, K.; Soboh, B.; Stripp, S.T. Infrared Characterization of the Bidirectional Oxygen-Sensitive [NiFe]-Hydrogenase from *E. coli*. *Catalysts* **2018**, *8*, 530. [[CrossRef](#)]

5. Kadowaki, M.A.S.; Godoy, M.; Kumagai, P.S.; Costa-Filho, A.; Mort, A.; Prade, R.A.; Polikarpov, I. Characterization of a New Glyoxal Oxidase from the Thermophilic Fungus *Myceliophthora thermophila* M77: Hydrogen Peroxide Production Retained in 5-Hydroxymethylfurfural Oxidation. *Catalysts* **2018**, *8*, 476. [[CrossRef](#)]
6. Park, Y.R.; Yoo, H.S.; Song, M.Y.; Lee, D.-H.; Lee, S.J. Biocatalytic Oxidations of Substrates through Soluble Methane Monooxygenase from *Methylosinus sporium* 5. *Catalysts* **2018**, *8*, 582. [[CrossRef](#)]
7. Li, F.; Zhuang, M.; Shen, J.; Fan, X.; Choi, H.; Lee, J.; Zhang, Y. Specific immobilization of *Escherichia coli* expressing recombinant glycerol dehydrogenase on mannose-functionalized magnetic nanoparticles. *Catalysts* **2019**, *9*, 7. [[CrossRef](#)]
8. Dzionek, A.; Dzik, J.; Wojcieszńska, D.; Guzik, U. Fluorescein Diacetate Hydrolysis Using the Whole Biofilm as a Sensitive Tool to Evaluate the Physiological State of Immobilized Bacterial Cells. *Catalysts* **2018**, *8*, 434. [[CrossRef](#)]
9. Arana-Peña, S.; Lokha, Y.; Fernández-Lafuente, R. Immobilization of Eversa Lipase on Octyl Agarose Beads and Preliminary Characterization of Stability and Activity Features. *Catalysts* **2018**, *8*, 511. [[CrossRef](#)]
10. Amaral-Fonseca, M.; Kopp, W.; Giordano, R.D.L.C.; Fernández-Lafuente, R.; Tardioli, P.W. Preparation of Magnetic Cross-Linked Amyloglucosidase Aggregates: Solving Some Activity Problems. *Catalysts* **2018**, *8*, 496. [[CrossRef](#)]
11. Xu, M.-Q.; Wang, S.-S.; Li, L.-N.; Gao, J.; Zhang, Y.-W. Combined Cross-Linked Enzyme Aggregates as Biocatalysts. *Catalysts* **2018**, *8*, 460. [[CrossRef](#)]
12. Kim, S.-J.; Kim, S.K.; Seong, W.; Woo, S.-G.; Lee, H.; Yeom, S.-J.; Kim, H.; Lee, D.-H.; Lee, S.-G. Enhanced (–)- α -Bisabolol Productivity by Efficient Conversion of Mevalonate in *Escherichia coli*. *Catalysts* **2019**, *9*, 432. [[CrossRef](#)]
13. Lee, J.H.; Cha, S.; Kang, C.W.; Lee, G.M.; Lim, H.G.; Jung, G.Y. Efficient Conversion of Acetate to 3-Hydroxypropionic Acid by Engineered *Escherichia coli*. *Catalysts* **2018**, *8*, 525. [[CrossRef](#)]
14. Baritugo, K.-A.; Kim, H.T.; Na Rhie, M.; Jo, S.Y.; Khang, T.U.; Kang, K.H.; Song, B.K.; Lee, B.; Song, J.J.; Choi, J.H.; et al. Construction of a Vitreoscilla Hemoglobin Promoter-Based Tunable Expression System for *Corynebacterium glutamicum*. *Catalysts* **2018**, *8*, 561. [[CrossRef](#)]
15. Xie, S.-S.; Zhu, L.; Qiu, X.-Y.; Zhu, C.-S.; Zhu, L.-Y. Advances in the Metabolic Engineering of *Escherichia coli* for the Manufacture of Monoterpenes. *Catalysts* **2019**, *9*, 433. [[CrossRef](#)]
16. Lee, H.-M.; Vo, P.N.L.; Na, D. Advancement of Metabolic Engineering Assisted by Synthetic Biology. *Catalysts* **2018**, *8*, 619. [[CrossRef](#)]
17. Sun, Y.; He, J.; Yang, G.; Sun, G.; Sage, V. A Review of the Enhancement of Bio-Hydrogen Generation by Chemicals Addition. *Catalysts* **2019**, *9*, 353. [[CrossRef](#)]
18. Mariyana, R.; Kim, M.-S.; Lim, C.I.; Kim, T.W.; Park, S.J.; Oh, B.-K.; Lee, J.; Na, J.-G. Mass Transfer Performance of a String Film Reactor: A Bioreactor Design for Aerobic Methane Bioconversion. *Catalysts* **2018**, *8*, 490. [[CrossRef](#)]

