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Editorial

Next-Generation Strategies in Fungal Bioconversion Process of Lignocellulosic Biomass-Derived Fuels and Chemicals: Targeted Multi-Omics and Substrate-Specific Platform

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Sustainable green bioethanol based on renewable plant biomass resources have emphasized as an ideal index for alternative plan due to the explosion of environmental damages (especially global warming) and fossil-based energy costs as well as the inappropriate use of food crops (here starch-based downstream process). Furthermore, the second generation process of the consolidated liquid fuel is based on large-scale platform with low cost. However, to materialize commercially available bioprocess, the effective depolymerization treatments of the recalcitrant materials are an integral part of entire bioconversion program for fermentable monomeric sugars, due to the enzymatic inaccessibility from sealed microfibril crystallinity and polymeric lignin complex [1]. Current interests of lignocellulose deconstruction process have been refocused on eco-friendly biocascade biosystem (without inhibitory byproducts; especially furfurals) using wood-degrading fungi (e.g.,basidiomycetes, ascomycetes, and anaerobic species) with various extracellular oxidative enzymes and cellulolytic hydrolase complexes instead of conventional methodology using physicochemical approaches (especially dilute acid, high temperature, and ammonia-soaking) [2–4]. However, the open access platform of only fungal biosystem to develop the hydrolysis efficiency of target substrates has not been undesirable for practical (or industrial) applications yet. Especially, it is hard for commercial processes to predominantly disrupt the substrates owing to the inevitable limitations (e.g., long-term cultivation, unstable cellular metabolism, programmed cell damage, and contaminable circumstance) of closed biological system [3–5]. Therefore, we will be able to identify at conserved biodegradation system, its process optimization (based on either useful targets or metabolic triggers) and comprehensive faculty (both intracellular signaling and extracellular metabolic interactions) in critical perspectives and possibly enhance are striction of conventional feasibility to seek synergistic effect and metabolic balance.

Interconnective comprehension of major (or minor) cellular regulatory and metabolic cascade is imperative for research in fundamental disciplines of efficient fungal-based biodegradable bioprocess. Biochemical signaling-related factors in downstream (or upstream) fungal bioprocess (based on mass balance of lignocellulosic feedstock) have been unveiled throughout over the past decades through painstaking examinations of individual inducible generations of metabolic products (or signaling precursors). Actually, the verification of entire networks as well as core pathways is extremely difficult in an acceptable understanding of whole-cell bioplatform level. Furthermore, genetic modification approaches on specific targets (or pathways) may semipermanently offer partial interpretation (regardless of inherent bias) of the fungal biosystem due to the cellular regeneration and bottleneck (by alternative routes) [2,6], and therefore it is unlikely for just current bottom-up concept to provide full understanding of multilayered biodegradable cascades.

Fungal systems biology for metabolic bioprocess optimization is a relatively new concept that emerged in the 21st century [6]. The first publications involved mostly omics tools (either microarrary or mass spectrometry-based analysis) which were used to verify target expression levels. Progressive areas of research include metabolomics and *in silico* fluxomics (additionally regulomics and signalomics) due to the emerging interest in metabolic intermediates and controllers within cells. However, the only single-omics approach has serious limitations, since they do not provide sufficient information for one to make definite decisions regarding the conspicuous regulatory system [7–9]. Very few double-omics studies were performed but their uses were also restricted to the verification and characterization of fungal bioprocess mechanisms [10–12]. Recently, newly-proposed multivariable omics (via three or more omics profiles) are being treated by the combination and integration of datasets from multi-omics pools (three or more omics profiles; e.g., genome, transcriptome, proteome, metabolome, and fluxome) to identifythe network cross linking of whole cell bioprocess [13,14]. Especially, based on simultaneous mass balance, target optimization (via statistical tools; mainly response surface methodology) of synergistic factors (e.g., ligninolytic peroxidases and cellulolytic hydrolases) in fungal conversion process can be significantly used to reduce complicated formalities of random omics information [10,13]. More remarkably, based on the targeted multiple omics program, the comprehensive map may be imparted novel links behind consolidated biodegradation mechanisms, and

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also provided a significant impact on improving the thermodynamic efficiency of subsequent biofuel production. Moreover, the top-down approach of utilizing target multi-omics to describe key bioprocess system will allow future metabolic engineering with a paradigm shift. On the other hand, it is too bad that the current unsatisfactory results have some glaring limitations, particularly by the controlling power (or driving force) of spontaneous homeostatic pathways via simultaneous metabolic adaptation [10,13]. Independent of target optimization of uncharacterized bioconversion process, it cannot be plausibly explained in terms of major repercussion and unique functionality. In this case, an addition of the other studies (e.g., computational fluxomics and bottom-up approaches) can provide the critical information to understand a reasonable mechanism regarding the downstream path of the underlying bioprocess.

In a view of the presence of preprocessed lignocellulosic fibrils, biocascading targets regarding the biological efficiency can contribute to the more aggressive cellulolytic process of external substrates. Until now, there are numerous reports of sequentially-combined platforms (e.g., milling, irradiation, water-soaking, and mild-chemical treatments) that appeared to be staged for the enzymatic digestibility and polymeric bioconversion with nearly-conventional time/cost effectiveness [4,15,16]. Based on biological metabolic systems (e.g., enzyme reactions, kinetics, and accessibilities) with either substrate-specificity or substrate-selectivity, the structural change (e.g., crystallinity index) of substrate components (mainly lignin, cellulose, and hemicellulose) is becoming one of the most influential methodological showcases in signaling convergence of substrate bioconversion yield by target microorganisms [13,16,17]. Preprocess combination has also been considered for the purpose of improving the conversion cost, which was partly achieved by performing simultaneous saccharification and fermentation in a consolidated program using fermentable microorganisms [18]. However, there is still a long way to go toward solution of the problems (especially practical productivities and long-term treatments) of fungal bioconversion as a conventional methodology.

In spite of newly introduced enterprising challenges regarding non-recombinant concept (here targeted multiple omics) and process optimization (here conserved biodegrading targets with substrate-specific activation), the economical advances of environmental friendly bioplatform need to be still developed in a conventional open-platform manner to aid reliable output costs. Particularly, the accessible possibility of large-scale bioprocess should be focused on the stably semipermanent production of high-energy fuels by cost-effective consolidated biosystem.

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