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Bio-based succinic acid and systems metabolic engineering, a brief review

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Abstract

Succinic acid, or butanedioic acid, is an intermediate of the tricarboxylic acid (TCA) cycle and an end product from anaerobic fermentation. This derivative acts as an important precursor and can be used in a wide range of industrial applications such as pharmaceuticals, food additives, biodegradable polymers, cosmetic products, cement additives, pigment, toner and green solvents. The development of systems metabolic engineering helps the biotechnologists to easily enhance the production of bio-based succinic acid.[1]

Keywords: Systems biology, Succinic Acid, Medium Optimization, Bio-based Chemical, Metabolic Engineering

Introduction

Biological systems are very complex, and a systematic approach is necessary to observe the diversity of interactions that can occur among molecular components of living cells. The use of genome-scale metabolic reconstructions of an organism can helps us to reduce this biological complexity and to elucidate the genotype-phenotype relationship. Today, the development of this approach has helped the biotechnologists to easily enhance the production of specific metabolites like succinic acid while other unnecessary ones are not producing or are limited. [2]

J. G. Zeikus et al. showed that *A. succinogenes*, with deletion of pyruvate formate lyase and formate dehydrogenase, succinate production doesn't improve. Only when donoring electron was electrically reduced neutral red or hydrogen, the *A. succinogenes* can use fumarate alone for succinate production. in *M. succiniciproducens* metabolic pathways that ends with acetate, formate, and lactate accumulation were deleted by disrupting the *ldhA*, *pflB*, *pta*, and *ackA* genes. In fed-batch fermentation with glucose feeding, this new *M. succiniciproducens* produced more succinate, with a yield of 0.76 g g^{-1} glucose and a productivity of 1.8 g L^{-1} h^{-1}. *E. coli* is one of the most attractive microorganisms for producing different metabolites due to availability of genetic tools, fast cell growth, and simple culture medium. Strategies in metabolic engineering of *E. coli* for succinate production can be classified as In the following: substrate improvement or product transportation, targeting the pathways directly involved in the succinate production, deletion of not nessesary pathways of by-products, and the combination of these methodes. These methods above have been studied in many reports and high efficient succinate producers have been constructed out of them (Ke-Ke Cheng et al. 2013). Overexpression of PEP carboxylase, PEP carboxykinase, pyruvate carboxylase, and malic enzyme, also was beneficial for succinic acid production (C. S. Millard et al. 1996). Yuto Yamauchi et al. harbored *Escherichia coli* transhydrogenase gene *pntAB* in *Corynebacterium glutamicum* and an improve in the final production rate of succinic acid was observed in comparison to transhydrogenase gene *udhA* (Yuto Yamauchi et al. 2014).

While metabolic engineering has become principal in bioengineering research and seems nessesary for producing bio-based succinic acid, a variety of computational tools such as metabolic flux analysis, metabolic control analysis (Soon Ho Hong 2007), MetaFluxNet (Sang jun Lee et al. 2005), Flux-sum analysis (Lakshmanan et al. 2015) and has been developed to improve our insight into the intracellular metabolic conditions through these years.

Results, Discussion, Conclusion and Suggestions

According to novel biotechnology science, bacterial medium compositions and the components themselves could be changed in a way for enhancing production amount or simplifying the downstream and separation process of the desired metabolite or biomass, but sometimes these changes could be effective on the other metabolites or also biomass production which might not always be favorable (Davami et al. 2015). So there is an individual formulation of the medium for each metabolite and it should not be used for another metabolite (Ritacco et al. 2018). Because of time-consuming and costly process of conventional medium formulation for a specific metabolite (Han et al. 2018), it is suggested to use systems biology approach to determine the optimum medium composition and avoid doing many labor-intensive experiments (Almo and Love 2014).

References

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