Bioresource Technology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Bioresource Technology

journal homepage: www.elsevier.com/locate/biortech

Review

Current status on metabolic engineering for the production of L-aspartate family amino acids and derivatives

Yanjun Li [a,b,c], Hongbo Wei [c], Ting Wang [c], Qingyang Xu [a,b,c], Chenglin Zhang [a,b,c], Xiaoguang Fan [a,b,c], Qian Ma [a,b,c], Ning Chen [a,b,c], Xixian Xie [a,b,c,*]

[a] National and Local United Engineering Lab of Metabolic Control Fermentation Technology, Tianjin University of Science and Technology, Tianjin 300457, China
[b] Key Laboratory of Microbial Engineering of China Light Industry, Tianjin University of Science and Technology, Tianjin 300457, China
[c] College of Biotechnology, Tianjin University of Science and Technology, Tianjin 300457, China

HIGHLIGHTS

- L-Aspartate family amino acids (AFAAs) are important in human and animal diet.
- Five-word strain breeding strategy "enter, flow, moderate, block, exit" are proposed.
- Genetic modifications in central metabolic pathways for AFAAs production.
- Metabolic pathways of AFAAs and derivatives and regulations involved.
- Metabolic engineering in AFAAs metabolic pathways based on different strategies.

ARTICLE INFO

Article history:
Received 28 March 2017
Received in revised form 20 May 2017
Accepted 22 May 2017
Available online xxxx

Keywords:
AFAA
Derivative
E. coli
C. glutamicum
Metabolic engineering

ABSTRACT

The L-aspartate amino acids (AFAAs) are constituted of L-aspartate, L-lysine, L-methionine, L-threonine and L-isoleucine. Except for L-aspartate, AFAAs are essential amino acids that cannot be synthesized by humans and most farm animals, and thus possess wide applications in food, animal feed, pharmaceutical and cosmetics industries. To date, a number of amino acids, including AFAAs have been industrially produced by microbial fermentation. However, the overall metabolic and regulatory mechanisms of the synthesis of AFAAs and the recent progress on strain construction have rarely been reviewed. Aiming to promote the establishment of strains of *Corynebacterium glutamicum* and *Escherichia coli*, the two industrial amino acids producing bacteria, that are capable of producing high titers of AFAAs and derivatives, this paper systematically summarizes the current progress on metabolic engineering manipulations in both central metabolic pathways and AFAA synthesis pathways based on the category of the five-word strain breeding strategies: enter, flow, moderate, block and exit.

Contents

* Corresponding author at: No. 29, 13th Avenue, Tianjin Economic and Technological Development Area (TEDA), Tianjin 300457, China.
E-mail address: xixianxie@tust.edu.cn (X. Xie).

http://dx.doi.org/10.1016/j.biortech.2017.05.145
0960-8524/

1. Introduction

Amino acids have been utilized for the production of food, feed, cosmetics and pharmaceuticals. Alternatively, amino acids and derivatives can be used for chemicals production to reduce fossil fuel consumption. Among the 20 proteinogenic amino acids, L-lysine, L-methionine, L-threonine and L-isoleucine are synthesized from L-aspartate, and these 5 amino acids are therefore called L-aspartate family amino acids (AFAAs). Except for L-aspartate, AFAAs are essential amino acids that cannot be synthesized by humans and most farm animals. This makes them important in the human and animal diet, and the global productions of the so-called feed amino acids L-lysine, DL-methionine, and L-threonine constitute the largest share (more than 50%) of the total amino acid market (Leuchtenberger et al., 2005). To date, a number of amino acids have been fermentatively produced and the annual production of amino acids has dramatically increased worldwide.

L-aspartate is at present industrially produced by enzymatic conversion of fumarate and ammonia using immobilized L-aspartase (E.C.4.3.1.1) or L-aspartase-containing microbial cells. Nevertheless, in 1980s, the main production method of L-aspartate was microbial fermentation, which is currently less competitive compared to the enzymatic method. DL-methionine, the presently added form in animal feed, is mainly produced by chemical synthesis from methyl mercaptan, acrolein, and hydrogen cyanide (Willke, 2014). With respect to the background of decreasing fossil resources and the stronger environmental constraints, alternative processes that are based on natural resources and more sustainable are gaining more and more interest. For example, CheilJedang (CJ) reported the enzymatic conversion of the fermentation-derived precursor succinyl homoserine (Kim et al., 2015) or acetyl homoserine (Hong et al., 2016) to produce L-methionine. Furthermore, microbial fermentation for L-methionine production has achieved great progress. This review

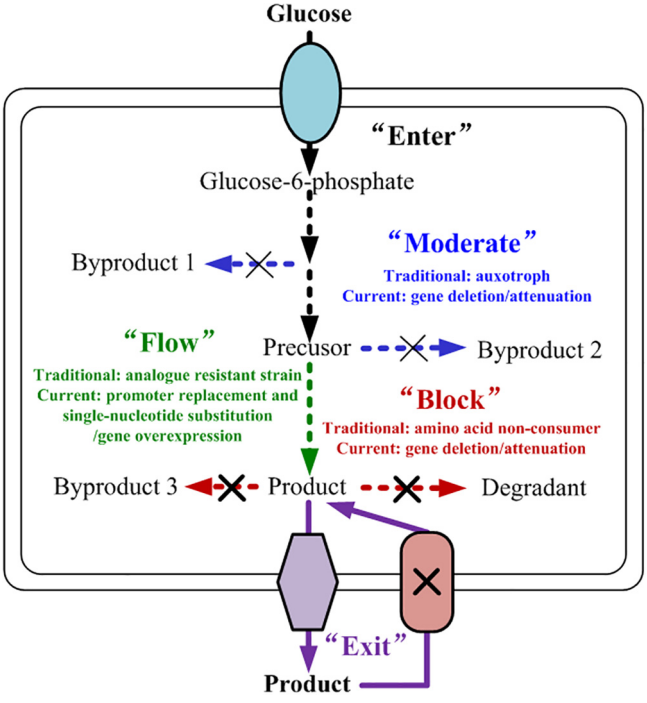

Fig. 1. Five-word strain breeding strategies: enter, flow, moderate, block, exit, and the traditional and molecular approaches involved.

Please cite this article in press as: Li, Y., et al. Current status on metabolic engineering for the production of L-aspartate family amino acids and derivatives. Bioresour. Technol. (2017), http://dx.doi.org/10.1016/j.biortech.2017.05.145