Research Progress in Enhancing Microbial Secondary Metabolites under Exogenous Stress

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Abstract

The target products of microbial fermentation accumulation are mainly secondary metabolites, such as antibiotics, hormones, alkaloids, toxins, etc. Microorganism's ability to produce secondary metabolites is weak, and the output is not enough to meet the industrial demand, so improving microbial secondary metabolites is an important problem for microbial fermentation. Exogenous stress can stimulate microbial cells to produce response mechanism and change their own metabolic flow to maintain their own survival. By means of short-term exogenous stress, microorganisms can regulate their own metabolic flow, enhance the secondary metabolic pathway, and up-regulate the expression of corresponding proteins, so that microorganisms can synthesize secondary metabolites efficiently.

Keywords

Exogenous Stress; Microorganism; Secondary Metabolites; Adaptive Evolution.

1. Introduction

In the 21st century, modern biotechnology develops rapidly through the basic research of biochemistry and molecular biology, and plays an increasingly important role in agriculture, food, medicine, environment and other fields. Modern biotechnology includes fermentation engineering, gene engineering, cell engineering, enzyme engineering and cell engineering[1]. Microbial fermentation refers to the process of transforming raw materials into products needed by human beings through specific metabolic pathways by using microorganisms under appropriate conditions. The application scope of fermentation engineering includes pharmaceutical industry, food industry, energy industry, chemical industry, agriculture and so on[2]. The production level of microbial fermentation mainly depends on the genetic characteristics and culture conditions of the strain itself.

2. Effects of short-term exogenous stress on microbial accumulation of secondary metabolitesSection Headings

The target products accumulated by microbial fermentation are mainly secondary metabolites, such as antibiotics, hormones, alkaloids, toxins, etc. Microorganism's ability to produce secondary metabolites is weak, and the output is not enough to meet the industrial demand, so improving microbial secondary metabolites is an important problem for microbial fermentation. Exogenous stress can stimulate microbial cells to produce response mechanism and change their own metabolic flow to maintain their own survival[3]. Short-term exogenous stress conditions of pressures in the microbial, microbial cells response to outside pressure to produce the corresponding response mechanism, under the pressure, the flow in the direction of the response to external pressure to enhance cell metabolism and corresponding metabolic pathway of protein expression, a corresponding increase in the number of secondary metabolites, microbial cell phenotypic changes and stable[4]. By means of short-term exogenous stress, microorganisms can regulate their own metabolic flow, enhance the secondary metabolic pathway, and up-regulate the expression of corresponding proteins, so that microorganisms can synthesize secondary metabolites efficiently[5].

2.1 Acid stress

In the process of microbial fermentation, pH, as one of the key factors in the fermentation process, has a great influence on the growth of microorganisms and the accumulation of products. When the microorganism is under stress, its physiological stress mechanism will respond in time to adapt to the growth pressure brought by the adverse environment. Short-term exogenous acid stress can stimulate the microorganism to produce a response mechanism to resist the external acid stress

2.2 Oxygen stress

Guobin Liang et al studied the effect of hydrogen peroxide-induced oxidative stress on glutathione (GSH) producing Candida. Based on the fact that hydrogen peroxide can effectively promote the accumulation of glutathione but inhibit cell growth, different concentrations of hydrogen peroxide stress (1 mmol/L at 4 h,2 mmol/L at 8 h, and 4 mmol/L at 12 h) maximized the production of glutathione.

2.3 Salt stress

Lipid can accumulate in microalgal cells under nutrient deficiency or other stress conditions, including salinity stress, which microalgae have specific mechanisms to adapt to[6]. For example, microalgal cells can accumulate solutes that protect osmosis, regulate ion exchange processes, produce antioxidant enzymes, and switch from active division to energy storage in the form of lipids. Abd el-Fatah Abomohra et al. isolated a species of halophilic microalgae, enhanced salt stress on the microalgae by increasing salinity, and further assessed the gradual adaptation of biomass and lipid production to increased salinity. In this study, the increase in salinity led to an increase in lipid content in batch culture, which reached a peak of 368.76 mg g− 1dW at 175%. In this study, the generation of oxidative stress led to the increase of MDA, CAT and SOD levels under the high salinity of D. salina KSA-HS022. The high activity of antioxidant enzymes under extreme salinity confirmed the ability of D. salina to resist oxidative stress under high salinity conditions. Under harsh conditions, microalgal cells alter intracellular lipid biosynthesis pathways toward accumulation of neutral lipids rather than synthesis of structural lipids. Thus, lipid accumulation by microorganisms growing under adverse conditions has been shown to be a defense mechanism against biotic or abiotic stresses[7]. Lipid synthesis increased in microalgal cells under salt stress, and intracellular lipid synthesis may be the mechanism of cell response to oxidative stress under salt stress.

2.4 Other coercion

Lignocellulosic biomass is a kind of abundant and sustainable raw material and a promising raw material for lactic acid production by microbial fermentation. However, toxic compounds that affect microbial growth and metabolism are released from the biomass by thermochemical pretreatment. So far, microbial sensitivity to biologically derived inhibitors remains a major obstacle to lignocellulosic lactic acid production. Martina Aulitto et al. demonstrated the feasibility of replacing the washing step with a complete cellular adaptation during the preculture of Bacillus coagulants MA-13. Compared with cells cultured with non-hydrolysate seeds, seeds cultured with pre-exposure to 30% hydrolysate reduced treatment time by 50%, increased average volume by 50% and average yield by 115%. The productivity stimulated in the hydrolysate-containing medium can be explained by the higher cellular energy demand induced by the stress response mechanism. Under anaerobic conditions, cells can produce excess energy in terms of adenosine triphosphate (ATP) and reducing capacity, only through enhanced sugar fermentation, resulting in an increase in lactic acid production. Microorganisms need a lot of energy to survive when they are stressed by exogenous inhibitors. Glycolysis may be a response mechanism produced by microorganisms to external stresses[8]. In response to exogenous inhibitors, the glycolysis pathway is enhanced and lactic acid production increases.

3. Long-term adaptive evolution to improve microbial secondary metabolites

Short-term exogenous stress changes the phenotype and phenotypic heterogeneity of microorganisms, and the phenotypes induced by microorganisms in the process of short-term adaptation can only play

a role under specific environmental factors[9]. The change of microbial phenotype is not enough to support the further research of microbial breeding. Long-term exogenous stress can perfectly solve this problem. Adaptive evolution and exogenous stress for a long time, called Adaptive evolution laboratory (the Adaptive laboratory evolution, the ALE), ALE technology usually come in a specific or superposition of selection pressure gradually as a benchmark to screen good performance of mutants, it is especially effective in enhancing microbial microbial resistance, in the long-term adaptation process, the microbes in exogenous stress for a long time will produce a series of changes in response to external stress genotype pressure, through the different type filter can get specific genes change evolutionary strains[10].

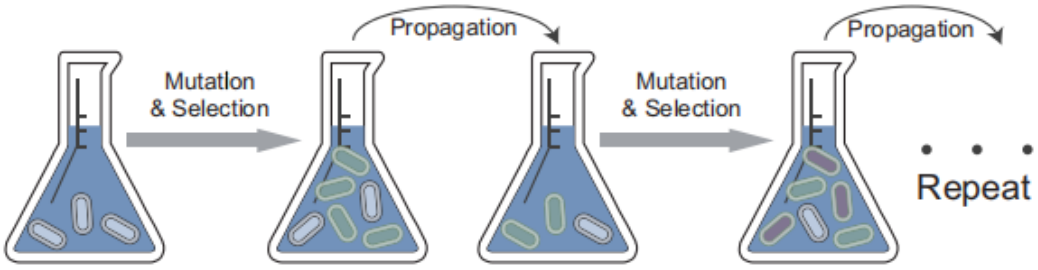

Fig. 1 Adaptive evolutionary process

4. Conclusion

In recent years, modern biotechnology occupies a more and more important position in various fields. Food, pharmaceutical, environment and agriculture all have great expectations for modern biotechnology. Microbial fermentation is a very important part of modern biotechnology. Low yield and high cost are the important factors limiting the development of microbial fermentation. The stress generated by exogenous stress can stimulate the microorganism to produce a response mechanism, so as to improve the ability of microorganism to resist exogenous stress. In the process of microbial resistance to exogenous pressure, the metabolic pathway changes accordingly, the metabolic pathway of related response mechanism is enhanced, and the synthesis of secondary metabolites is improved.

As DNA sequencing and bioinformatics and genetic engineering technology such as the development of external stress and microbial fermentation has become increasingly important in microbial breeding, exogenous stress forced microbial response phenotype and gene level changes, DNA sequencing and gene engineering to study the response mechanism of microorganism, for subsequent further realize the directional genetically engineered strains for new intervention target and direction.

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