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Current Synthetic and Systems Biology

Commentary

Types of Production Systems for Synthetic Drugs

Statin Brilan*

Department of Biotechnology, Thomas Jefferson University, Philadelphia, Pennsylvania, USA

DESCRIPTION

The advancement of synthetic biology has made it possible to utilize a variety of platforms to express heterologous genes. This technique has evolved into a significant method for producing target pharmaceuticals. Natural product medications offer a wide variety of uses in the treatment of many ailments, according to new clinical investigations. To address the requirement for various recombinant pharmaceuticals, an effective expression method is necessary. There is currently no common substrate for heterologous expression of different kinds of metabolites. The *E. coli* expression system is the most often used microbial expression system. The expression systems of *B. Subtilis*, yeast, and filamentous fungi are the first two systems are the most often used prokaryotic host bacteria, whereas the other two are commonly utilized for eukaryotic expression. Understanding the biosynthetic mechanism enables the sensible selection and use of these expression systems for the expression of secondary metabolite biosynthetic gene clusters.

Prokaryotic expression systems

For the synthesis of recombinant proteins, *Escherichia coli* are the chosen bacterium. *E. coli* is primarily utilized for cloning, genetic modification, and small-scale manufacturing and the principles behind these operations have been extensively researched. Because of its highly defined genetic background, quick reproduction, low cost, high expression level, reliable 2H/13C/15N isotope labeling technology, and a wide variety of applications, *E. coli* has been frequently employed in the study of heterologous therapeutic proteins. *E. coli* is a prokaryote; it lacks a regulatory mechanism for eukaryotic gene expression and the capacity to catalyze Post Translational Modifications (PTMs), particularly those mediated by cytochrome P450 enzymes, which significantly restricts its applicability as a recombinant drug factory.

Yeast expression systems

Since yeast is the simplest eukaryotic organism, it is more suitable than prokaryotes for the production of active eukaryotic proteins and can perform posttranslational modifications such as signal peptide proteolysis, disulfide bond formation, and glycosylation. Yeast, in particular, is better suited for eukaryotic cytochrome oxidoreductase gene expression. *S. cerevisiae* offers distinct advantages in physiological properties important to commercial ethanol production, including pH tolerance, high ethanol concentrations, high sugar content, and high osmotic pressure. Many products on the market are made with *S. cerevisiae*, including artemisinic acid, taxadiene, noscapine etc. However, due to low protein production, excessive glycosylation of glycoproteins, plasmid instability, and restricted quantities of building blocks, commercial *S. cerevisiae* products have limited utility. *Yarrowia lipolytica*, non-conventional yeast, has been widely studied and considered a promising host for natural product synthesis. As an industrial host, this yeast offers various benefits, including the ability to grow normally on low-cost substrates (such as sugars, lignocellulose, fatty acids, lipids, waste oils, and crude glycerol) and under high-stress circumstances (organic acids, hyper salinity, and metal stresses).

Filamentous fungal expression systems

A large fraction of the secondary metabolite biosynthetic gene cluster has been expressed heterologously in the yeast *S. cerevisiae* and the filamentous fungus *Aspergillus oryzae* and *Aspergillus nidulans*. Filamentous fungi have a high capacity to produce and release recombinant proteins, as well as posttranslational processing capabilities like glycosylation, protease cleavage, and disulfide bond formation in heterologous proteins. Many fungal hosts used for heterologous expressions, such as *A. niger* and *A. oryzae*, are safe and have been used for a long time in the food and food processing sectors; these species offer certain distinct benefits. First, such fungal hosts may express a full gene cluster of natural fungal product biosynthesis, and the introns are appropriately spliced in the gene cluster; consequently, intron removal is unnecessary. Furthermore, the filamentous fungus can generate target products at a low cost. For example, heterologous expression in the filamentous fungus can result in a large production of multi-active enniatin.

Correspondence to: Dr. Statin Brilan, Department of Biotechnology, Thomas Jefferson University, Philadelphia, Pennsylvania, USA, E-mail: Stabrl@gamil.com

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CONCLUSION

Research and technical advancement in this new subject can offer the required basis for the biotechnology industry's commercial sustainability. It is also clear from the preceding discussion that we have not entirely accomplished this and that there are still many hurdles to overcome. One of the major barriers to route reconstruction for plant natural products is a lack of understanding of biosynthetic processes. Due to a lack of knowledge of multienzyme interaction, compartmentalization, or metabolic control, the yields of natural products using reconstructed biosynthetic approaches cannot match the parameters for large-scale production. Furthermore, we must optimize more broad hosts to swiftly scale up the production level of target pharmaceuticals. If it continues to progress at its current rate, synthetic biology of natural pharmaceuticals will soon reach mass manufacturing and the market.