Perspective
Volume 15:01, 2025

Journal of Bioprocessing & Biotechniques

ISSN: 2155-9821 Open Access

Yeast and Fungi as Eukaryotic Expression Systems for Biologics Production

Kang Ojer*

Department of Biochemistry and Systems Biology, University of Liverpool, Liverpool, UK

Introduction

The production of biologics, including therapeutic proteins, vaccines, and enzymes, relies on efficient expression systems that can ensure high yields, proper post-translational modifications, and cost-effective manufacturing. Among the various expression platforms available, yeast and fungi have emerged as powerful non-mammalian eukaryotic hosts for biologics production. These microorganisms offer a combination of rapid growth, ease of genetic manipulation, and the ability to perform post-translational modifications, making them suitable for the large-scale production of recombinant proteins. Their use spans multiple industries, from pharmaceuticals to industrial biotechnology, where they play a crucial role in meeting global demands for biologics. Yeast, particularly *Saccharomyces cerevisiae* and *Pichia pastoris*, is widely utilized as a host organism for recombinant protein production. *Saccharomyces cerevisiae*, commonly known as baker's yeast, has a long history in biotechnology and has been extensively studied for its genetic stability and expression capabilities. It offers the advantage of eukaryotic protein processing, including glycosylation, disulfide bond formation, and proper protein folding. Its well-characterized genome and availability of genetic tools make it an attractive system for the production of biologics. However, one of its major limitations is its tendency to hyperglycosylate proteins, which can impact the functionality and therapeutic efficacy of certain biologics.

Description

Pichia pastoris has gained prominence as a superior yeast expression system due to its ability to perform more human-like glycosylation patterns while maintaining high-level expression of recombinant proteins. This methylotrophic yeast can utilize methanol as a carbon source, enabling strong induction of foreign gene expression under the control of the Alcohol Oxidase (Aox) Promoter. The secretion of recombinant proteins into the culture medium simplifies downstream processing, reducing production costs. Additionally, *Pichia pastoris* can grow to high cell densities in bioreactors, further increasing protein yields. These advantages make it an important expression system for the production of monoclonal antibodies, vaccine antigens, and industrial enzymes. Filamentous fungi, including species from the genera *Aspergillus*, *Trichoderma*, and *Fusarium*, have also been explored as expression hosts for biologics. Their natural ability to secrete large amounts of proteins makes them particularly valuable for industrial enzyme production. *Aspergillus niger* and *Aspergillus oryzae* are widely used for the production of food-grade and pharmaceutical enzymes due to their high secretion capacity and ability to grow on inexpensive substrates. Fungal expression systems provide advantages in post-translational modifications, including glycosylation, phosphorylation, and proteolytic processing, which are essential for the functionality of many biologics. One of the key benefits of yeast and fungal expression systems is their ability to scale up production with relatively low costs compared to mammalian cell cultures. Yeast and fungi can be cultivated in simple media without the need for expensive growth factors or serum supplementation, reducing the overall cost of production. Furthermore, their robustness allows them to withstand harsh fermentation conditions, making them suitable for large-scale bioprocessing. The use of fed-batch and continuous fermentation strategies in bioreactors enables high cell densities and prolonged production cycles, further enhancing productivity [1].

The post-translational modifications performed by yeast and fungi are a crucial consideration in biologics production. While these systems can carry out glycosylation, the glycan structures they produce differ from those in mammalian cells. For therapeutic proteins, glycosylation plays a significant role in stability, activity, and immunogenicity. Efforts to engineer yeast and fungal glycosylation pathways have led to the development of glycoengineered strains that produce human-like glycan structures. For example, *Pichia pastoris* strains have been modified to express human glycosyltransferases, allowing the production of recombinant proteins with glycosylation patterns more compatible with human biology. These advancements improve the therapeutic potential of biologics produced in yeast and fungi. In vaccine production, yeast has played a pivotal role in generating recombinant vaccine antigens. The hepatitis B vaccine was one of the first recombinant vaccines produced using Saccharomyces cerevisiae, demonstrating the feasibility of yeast-based vaccine production. Since then, yeast has been employed in the production of other vaccines, including those for human papillomavirus (HPV) and malaria. The ability of yeast to produce Virus-Like Particles (VLPs) has made it a valuable system for vaccine development, as VLPs closely mimic native viruses and elicit strong immune responses. The rapid scalability of yeast-based vaccine production is especially advantageous in responding to emerging infectious diseases [2].

Fungal expression systems are also being explored for their potential in producing therapeutic proteins, including cytokines, growth factors, and hormones. Aspergillus and Trichoderma species have been engineered to express heterologous proteins, and their ability to secrete high amounts of recombinant proteins simplifies purification processes. The use of fungal systems in pharmaceutical production continues to expand as researchers optimize expression platforms for improved yields and product quality. Despite their advantages, yeast and fungal expression systems face certain challenges that require further optimization. Protein folding and secretion can be affected by the host's endogenous proteases, leading to protein degradation. Strategies such as protease-deficient strains and co-expression of chaperones have been employed to enhance protein stability and yield. Additionally, some proteins may require complex folding pathways that are not naturally present in yeast or fungi, necessitating further strain engineering and process optimization [3].

Recent advances in synthetic biology and metabolic engineering have significantly improved the capabilities of yeast and fungal expression systems. The use of CRISPR-Cas9 genome editing has facilitated precise genetic modifications, allowing researchers to optimize metabolic pathways for increased protein expression. Synthetic promoters, regulatory elements, and secretion signals have been engineered to fine-tune gene expression and enhance protein secretion. These innovations continue to expand the potential of yeast and fungi as versatile platforms for biologics production. Environmental sustainability is another factor driving the interest in yeast and

***Address for Correspondence:** Kang Ojer, Department of Biochemistry and Systems Biology, University of Liverpool, Liverpool, UK, E-mail: Ojerkang@gmail.com*

Received: 02 January, 2025, Manuscript No. Jbpbt-25-162102; **Editor Assigned:** 04 January, 2025, Pre QC No. P-162102; **Reviewed:** 17 January, 2025, QC No. Q-162102; **Revised:** 23 January, 2025, Manuscript No. R-162102; **Published:** 31 January, 2025, DOI: 10.37421/2155-9821.2025.15.663

fungal expression systems. Compared to mammalian cell cultures, yeast and fungi require fewer resources, produce lower greenhouse gas emissions, and generate less waste. Their ability to grow on renewable feedstocks, including agricultural byproducts and lignocellulosic biomass, makes them attractive candidates for sustainable biomanufacturing. The development of circular bioeconomy strategies, where waste materials are converted into valuable biologics, aligns with global sustainability goals and reduces the environmental impact of biopharmaceutical production [4].

The regulatory landscape for yeast- and fungi-derived biologics continues to evolve as more products enter the market. Regulatory agencies, including the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), require stringent quality control measures to ensure the safety, efficacy, and consistency of biologics. Advances in analytical techniques, including mass spectrometry and glycan profiling, have enabled better characterization of recombinant proteins, facilitating regulatory approval. The establishment of Good Manufacturing Practices (GMP) and quality assurance protocols further supports the commercialization of yeast- and fungi-based biologics. Looking ahead, the integration of yeast and fungal expression systems with emerging biotechnologies, such as Artificial Intelligence (AI)-driven bioprocess optimization and machine learning-guided strain engineering, will further enhance their efficiency and productivity. AI-driven approaches can predict optimal fermentation conditions, streamline protein purification, and accelerate strain development. The combination of computational biology and experimental research will continue to push the boundaries of biologics production, making yeast and fungi even more valuable in the biopharmaceutical industry [5].

Conclusion

In conclusion, yeast and fungi have established themselves as indispensable eukaryotic expression systems for the production of biologics. Their advantages, including cost-effective cultivation, scalability, and post-translational modification capabilities, make them ideal hosts for recombinant protein production. Advances in genetic engineering, synthetic biology, and bioprocess optimization have further expanded their potential, enabling the production of high-quality therapeutics, vaccines, and industrial enzymes. While challenges such as glycosylation differences and protein folding persist, ongoing research continues to address these limitations, paving the way for more efficient and sustainable biologics production. As the demand for biologics continues to grow, yeast and fungal expression systems will remain at the forefront of biotechnology, offering innovative solutions for the pharmaceutical and industrial sectors.

Acknowledgement

None.

Conflict of Interest

None.

References

1. Meier, Jordan L. and Michael D. Burkart. "The chemical biology of modular biosynthetic enzymes." Chem Soc Rev 38 (2009): 2012-2045.
2. Williams, Gavin J. "Engineering polyketide synthases and nonribosomal peptide synthetases." Curr Opin Struct Biol 23 (2013): 603-612.
3. Wang, Jie, Keke Fei, Hua Jing and Zhihai Wu, et al. "Durable blockade of PD-1 signaling links preclinical efficacy of sintilimab to its clinical benefit." Chem Soc Rev 11 (2019): 1443-1451.
4. McMahon, Conor, Alexander S. Baier, Roberta Pascolutti and Marcin Wegrecki, et al. "Yeast surface display platform for rapid discovery of conformationally selective nanobodies." Nat Struct Mol Biol 25 (2018): 289-296.
5. Ardiani, Andressa, Jack P. Higgins and James W. Hodge. "Vaccines based on whole recombinant Saccharomyces cerevisiae cells." FEMS Yeast Res 10 (2010): 1060-1069.

How to cite this article: Ojer, Kang. "Yeast and Fungi as Eukaryotic Expression Systems for Biologics Production." *J Bioprocess Biotech* 15 (2025): 663.