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Alkali-regulated synthetic promoters: a new tool for efficient protein production in yeast



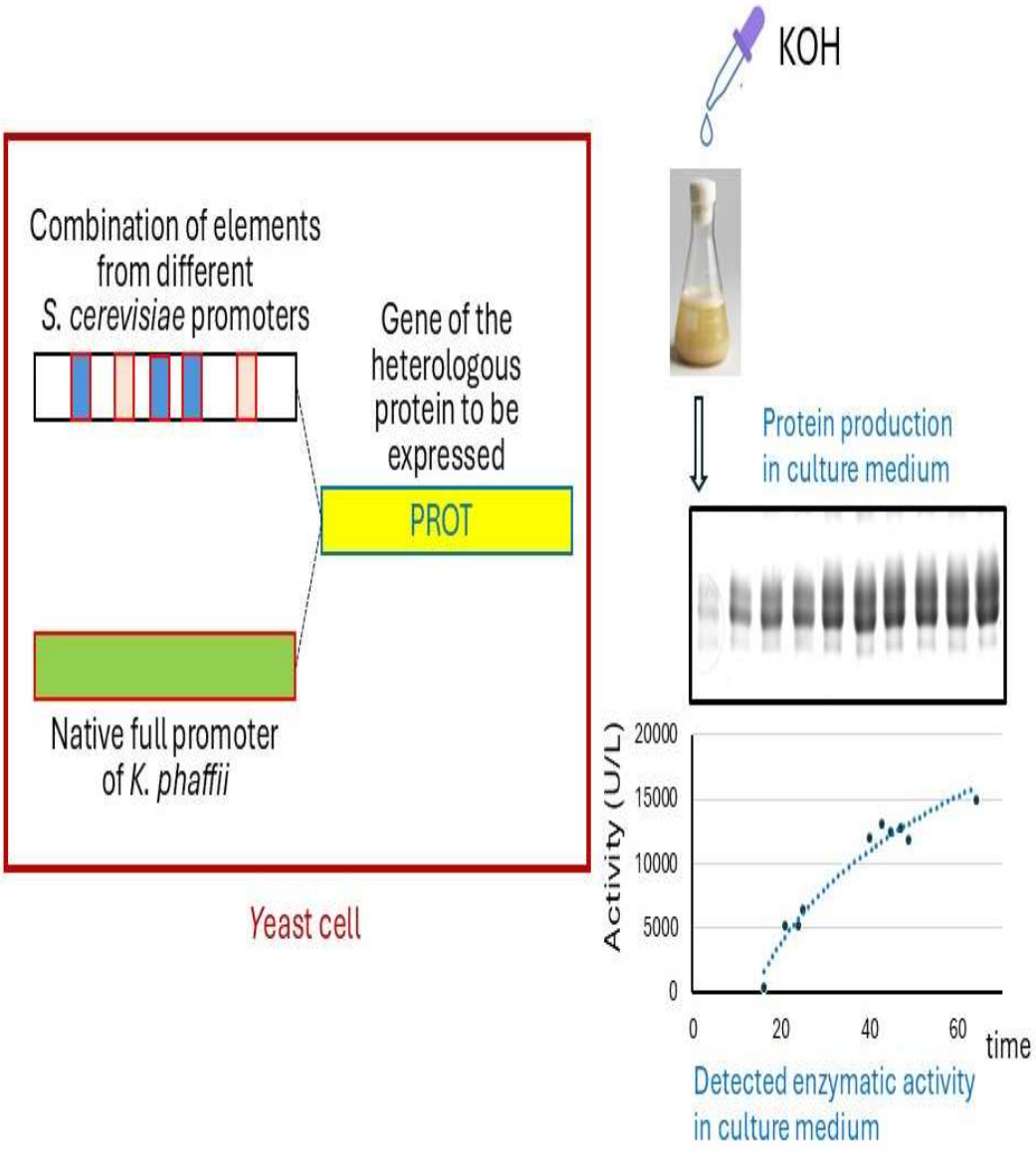
The Yeast Molecular Biology Group has developed regulators that can be activated by alkaline pH in yeasts capable of directing protein expression regardless of the carbon source. These results allow the optimization of protein production under industrial conditions and reinforce the role of yeast as key platforms in modern biotechnology.

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Nowadays, most proteins of industrial or biomedical interest are obtained through recombinant DNA techniques and heterologous expression in microorganisms. Yeasts, as eukaryotic microorganisms, are widely used platforms for these purposes. In this context, the development of regulatable promoters capable of driving protein expression regardless of the carbon source has been an active research field for years.

Our Yeast Molecular Biology Group at the Institute of Biotechnology and Biomedicine (IBB) of the Universitat Autònoma de Barcelona (UAB), with a long-standing trajectory on this subject, has recently published two articles that represent a significant advance in this field, focusing on promoters regulated by alkalinization of the medium.

In the first article, published in *Microbial Biotechnology* (Zekhnini et al. 2025, the brewer's yeast *Saccharomyces cerevisiae* was used as a host to develop a strategy for constructing synthetic promoters. These promoters consist of combinations of short DNA sequences containing transcriptional regulatory elements that are activatable under alkaline pH conditions. We showed that they can be advantageously used compared to existing systems to express laccase, an enzyme of industrial interest in the treatment of wood lignin, for example in the paper industry. Notably, the system is activated simply by adding potassium hydroxide (KOH) to the medium, facilitating its application in industrial processes without changing the carbon source or modifying other culture conditions.



In a previous publication (Albacar et al. 2024), we had identified native promoters inducible by alkaline pH in *Komagataella phaffii* (formerly known as Pichia pastoris), a yeast of great relevance in industrial enzyme production, demonstrating that these promoters could be exploited for heterologous protein expression. In the recent publication in *Scientific Reports* (Albacar et al. 2025), key components of the signaling pathways governing the expression of these alkaline pH-inducible promoters are elucidated using CRISPR-Cas9, RNA-seq and proteomics techniques. The study analyzes the impact of mutations in two

transcription factors, Rim101 and Crz1, and concludes that Rim101 regulates at least 50% of the response to medium alkalinization, making it a promising target for process optimization.

These advances pave the way to more efficient systems adapted to real industrial conditions and reinforce the role of yeast as key platforms in modern biotechnology.

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