

## RESEARCH ARTICLE

# Genetic modules for $\alpha$ -factor pheromone controlled growth regulation of *Saccharomyces cerevisiae*

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**Funding information**

Europäischer Sozialfond (ESF) and the Free State of Saxony within the KoSyn project with the SAB grant number, Grant/Award Number: 100382367

**Abstract**

*Saccharomyces cerevisiae* is a commonly used microorganism in the biotechnological industry. For the industrial heterologous production of compounds, it is of great advantage to work with growth-controllable yeast strains. In our work, we utilized the natural pheromone system of *S. cerevisiae* and generated a set of different strains possessing an  $\alpha$ -pheromone controllable growth behavior. Naturally, the  $\alpha$ -factor pheromone is involved in communication between haploid *S. cerevisiae* cells. Perception of the pheromone initiates several cellular changes, enabling the cells to prepare for an upcoming mating event. We exploited this natural pheromone response system and developed two different plasmid-based modules, in which the target genes, *MET15* and *FAR1*, are under control of the  $\alpha$ -factor sensitive *FTG1* promoter for a controlled expression in *S. cerevisiae*. Whereas expression of *MET15* led to a growth induction, *FAR1* expression inhibited growth. The utilization of low copy number or high copy number plasmids for target gene expression and different concentrations of  $\alpha$ -factor allow a finely adjustable control of yeast growth rate.

**KEYWORDS**

growth regulation, pheromone response, *Saccharomyces cerevisiae*, synthetic biology,  $\alpha$ -factor

## 1 | INTRODUCTION

Due to the easy genetic tractability and the extensive knowledge regarding its metabolism, genetics and lifestyle, the yeast *Saccharomyces cerevisiae* is a commonly applied microorganism in the biotechnological industry, for example, for beverage, food or biofuel production [1–3]. For

maintaining stability in biotechnological production cultures or co-cultures, one critical point is the controllable growth behavior of the microorganisms. In general, yeast growth can be controlled by the availability of nutrients such as sugars, amino acids, or nitrogen compounds, as these determine development programs and growth rates [4]. Different compounds such as farnesol [5], proteinogenic amino acids as well as the nonproteinogenic amino acids citrulline and ornithine [6], or weak acids like acetic acid or formic acid [7] possess growth-inhibiting effects at high levels. For some applications, the use of specific mutations may also be an alternative constitutive

**Abbreviations:** GPCR, protein-coupled receptor; HA<sub>3</sub>, three copies of the viral hemagglutinin protein tag; Mw calc., calculated molecular weight; RLU, relative nephelometric units; *S. cerevisiae*, *Saccharomyces cerevisiae*.

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