Engineering prokaryotic transcriptional activators as metabolite biosensors in yeast

Whole-cell biocatalysts have proven a tractable path toward sustainable production of bulk and fine chemicals. Yet the screening of libraries of cellular designs to identify best-performing biocatalysts is most often a low-throughput endeavor. For this reason, the development of biosensors enabling real-time monitoring of production has attracted attention. Here we applied systematic engineering of multiple parameters to search for a general biosensor design in the budding yeast Saccharomyces cerevisiae based on small-molecule binding transcriptional activators from the prokaryote superfamily of LysR-type transcriptional regulators (LTTRs). We identified a design supporting LTTR-dependent activation of reporter gene expression in the presence of cognate small-molecule inducers. As proof of principle, we applied the biosensors for in vivo screening of cells producing naringenin or cis,cis-muconic acid at different levels, and found that reporter gene output correlated with production. The transplantation of prokaryotic transcriptional activators into the eukaryotic chassis illustrates the potential of a hitherto untapped biosensor resource useful for biotechnological applications.

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