An Orthogonal and pH-Tunable Sensor-Selector for Muconic Acid Biosynthesis in Yeast - DTU Orbit (19/08/2019)

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Microbes offer enormous potential for production of industrially relevant chemicals and therapeutics, yet the rapid identification of high-producing microbes from large genetic libraries is a major bottleneck in modern cell factory development. Here, we develop and apply a synthetic selection system in Saccharomyces cerevisiae that couples the concentration of muconic acid, a plastic precursor, to cell fitness by using the prokaryotic transcriptional regulator BenM driving an antibiotic resistance gene. We show that the sensor-selector does not affect production nor fitness, and find that tuning pH of the cultivation medium limits the rise of nonproducing cheaters. We apply the sensor-selector to selectively enrich for best-producing variants out of a large library of muconic acid production strains, and identify an isolate that produces more than 2 g/L muconic acid in a bioreactor. We expect that this sensor-selector can aid the development of other synthetic selection systems based on allosteric transcription factors.

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