The global regulator enhances organic solvent tolerance and Δ^1-dehydrogenation productivity of *Arthrobacter simplex*

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The Steroidal hormones are the second largest class of drugs after antibiotics, which are generally produced by microbial transformation. During bioconversion process, organic solvents are widely used for facilitating hydrophobic substrate dissolution in industry. Thus, strains that tolerate organic solvents are highly desirable. A variety of efforts have been made to enhance the organic solvent tolerance of microorganisms, but the enhancement in the tolerance is still a difficult task because the phenotype is, in many cases, a result of multigene regulation. Recently, the introduction of global regulators has been promising for organic solvent tolerance improvement since they directly or indirectly manipulate the transcriptional regulatory network.

IrrE, a global regulator, derived from *Deinococcus radiodurans*, was firstly introduced into *Arthrobacter simplex* with Δ^1 -dehydrogenation ability. The results evidenced that IrrE did not affect cell biological traits and biotransformation performance under non-stress conditions. However, the recombinant strain achieved a productivity higher than that of the control strain in systems containing more ethanol and substrate, which coincided with cell viability under ethanol stress, the major stress factor during biotransformation. It also demonstrated that IrrE caused genome-wide transcriptional perturbation, and several defense proteins or systems were linked with higher organic solvent tolerance. IrrE simultaneously enhanced cell resistance to various stresses, and its horizontal impacts showed strain and stress dependence. In conclusion, the introduction of exogenous global regulators is an efficient approach to enhance organic solvent tolerance in steroid-transforming strains, resulting in higher productivity. Our results also implied that IrrE might act as a practical regulatory "part" that operates at a level of complexity much higher than those of local regulators or functional genes in the view of synthetic biology, which would be useful for eliciting cellular tolerances that were otherwise difficult to improve by manipulating individual genes or pathways.

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Research Interests:

Screening, modification and application of microorganisms with important values in medicine, food and environment fields

Biotransformation and Biochemical Engineering

Synthetic Engineering

Selected publications

1. Luo et al., *Applied Microbiology and Biotechnology*, 2018, 102: 9331-9350.
2. Song et al., *Journal of Agricultural and Food Chemistry*, 2018,66(20): 5210-5220.