

Efficient 3-hydroxypropionic acid production by biosensor-based evolutionary engineering of aldehyde dehydrogenase

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3-Hydroxypropionic acid (3-HP) is an important platform chemical, and biological production of 3-HP from glycerol as a carbon source using glycerol dehydratase (GDH) and aldehyde dehydrogenase (ALDH) has been revealed to be effective because of simple pathway and higher yield and productivity. However, 3-HP production from glycerol have problem of low activity and inactivation of GDH and ALDH. For evolutionary protein engineering, 3-HP responsive transcription factor based biosensor was constructed and applied to an ALDH library, specifically aldehyde-binding site library of alpha-ketoglutaric semialdehyde dehydrogenase (KGSADH). Only two serial cultures resulted in enrichment of strains showing increased 3-HP production, and an isolated KGSADH variant enzyme exhibited a 2.79-fold higher catalytic efficiency toward its aldehyde substrate than the wild-type one. Our approach provides the simple and efficient tool to engineer the pathway enzymes in metabolic engineering.