Secretive glutamate decarboxylase of Corynebacterium glutamicum catalyzes an efficient conversion of glutamic acid to γ-aminobutyric acid

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Abstract

γ-Aminobutyric acid (GABA) is a non-protein amino acid produced from the decarboxylation of glutamate by glutamate decarboxylase. Corynebacterium glutamicum is the most promising host of γ-aminobutyric acid production for its inherent glutamate precursor supply. However, the intracellularly expressed glutamate decarboxylase in C. glutamicum showed the weak catalysis capacity on the conversion of glutamate to γ-aminobutyric acid. Here we designed an different catalysis scenario by secretively overexpressing the glutamate decarboxylase in C. glutamicum and moving the decarboxylation reaction into the extracellular space for GABA synthesis. A signal peptide in the expression cassette directed the successful secretion of glutamate decarboxylase in C. glutamicum. The extracellular catalysis by secreted glutamate decarboxylase increased the γ-aminobutyric acid generation by three-folds, comparing with that by intracellular catalysis. Further efforts on enhancing the expression of glutamate decarboxylase and decreasing the degradation of γ-aminobutyric acid improved γ-aminobutyric acid generation by 39%. The fed-batch fermentation of the engineered C. glutamicum strain reached the record high titer (77.6g /L), overall yield (0.37 g/g glucose), and productivity (1.21 g/L/h) of γ-aminobutyric acid production. This study demonstrated a unique design of extracellular catalysis for efficient γ-aminobutyric acid production by C. glutamicum.

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