

Synthetic N-terminal coding sequences for fine-tuning gene expression and metabolic engineering in *Bacillus subtilis*

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N-terminal coding sequences (NCSs) of genes significantly influence gene expression at the translation level and are important for fine-tuning gene expression in bacteria, however, engineering NCSs to fine-tune metabolic pathways is challenging. Here, we developed a statistics-guided native and synthetic NCSs engineering approach to fine-tune gene expression in the industrially important microorganism *Bacillus subtilis*. This method is based on experimentally characterizing and statistically analyzing 96 rationally selected NCSs from *B. subtilis* endogenous genes. These NCSs exhibited a magnitude difference of greater than 4 orders in their ability to drive gene expression in 4 different dynamic patterns, including growth-coupled, growth-delayed, consistent expression, and inhibitory patterns. Synthetic and native NCSs were used to fine-tune expression of key enzymes, identified via pathway analysis and kinetic modeling, in the biosynthetic pathway of the useful nutraceutical *N*-acetylneuraminic acid (NeuAc). We observed a 3.21-fold improvement in NeuAc biosynthesis, indicating that NCSs can provide a synthetic biology toolbox to fine-tune gene expression for metabolic engineering.

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Education:

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Research Interests:

Metabolic engineering for nutraceutical biosynthesis

Synthetic biology tool development for fine-tuning pathway

Selected publications

1. Liu et al., *Nature Communications*, 2016, 7:11933.
2. Liu* et al., *Trends in Biotechnology*, 2019, 37:548-562.
3. Liu* et al., *Metabolic Engineering*, 2019, 55:131-141.