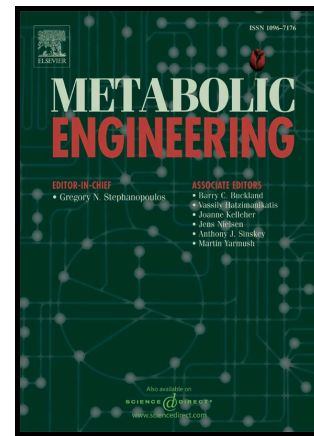


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Boosting heterologous protein production yield by adjusting global nitrogen and carbon metabolic regulatory networks in *Bacillus subtilis*

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Abstract

Bacillus subtilis is extensively applied as a microorganism for the high-level production of heterologous proteins. Traditional strategies for increasing the productivity of this microbial cell factory generally focused on the targeted modification of rate-limiting components or steps. However, the longstanding problems of limited productivity of the expression host, metabolic burden and non-optimal nutrient intake, have not yet been completely solved to achieve significant production-strain improvements. To tackle this problem, we systematically rewired the regulatory networks of the global nitrogen and carbon metabolism by random mutagenesis of the pleiotropic transcriptional regulators CodY and CcpA, to allow for optimal nutrient intake,

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