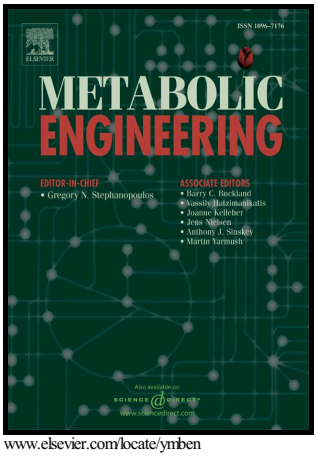

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Bioconversion of methane to C-4 carboxylic acids using carbon flux through acetyl-CoA in engineered *Methylomicrobium buryatense* 5GB1C

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ABSTRACT

Methane, the primary component of natural gas, is the second most abundant greenhouse gas (GHG) and contributes significantly to climate change. The conversion of methane to industrial platform chemicals provides an attractive opportunity to decrease GHG emissions and utilize this inexpensive and abundantly available gas as a carbon feedstock. While technologies exist for chemical conversion of methane to liquid fuels, the technical complexity of these processes mandate high capital expenditure, large-scale commercial facilities to leverage economies of scale that cannot be efficiently scaled down. Alternatively, bioconversion technologies capable of efficient small-scale operation with high carbon and energy efficiency can enable deployment at remote methane resources inaccessible to current chemical technologies. Aerobic obligate methanotrophs, specifically *Methylomicrobium buryatense* 5GB1, have recently garnered increased research interest for development of such bio-technologies. In this study, we demonstrate production of C-4 carboxylic acids non-native to the host, specifically crotonic and butyric acids, from methane in an engineered *M. buryatense* 5GB1C by diversion of carbon flux through the acetyl-CoA node of central 'sugar' linked metabolic pathways using reverse β-oxidation pathway genes. The synthesis of short chain carboxylic acids through the acetyl-CoA node demonstrates the potential for engineering *M. buryatense* 5GB1 as a platform for bioconversion of methane to a number of value added industrial chemicals, and presents new opportunities for further diversifying the products obtainable from methane as the feedstock.

KEYWORDS: *Methylomicrobium buryatense;* methanotroph; crotonic acid; butyric acid; gas-to-liquid conversion; one carbon feedstocks

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