Engineered metabolism for chemical production from one-carbon substrates

Ramon Gonzalez, Department of Chemical & Biomedical Engineering, University of South Florida
ramongonzale@usf.edu

Key Words: C1 feedstocks, native & synthetic methylotrophy, Methylomicrobium buryatense, Escherichia coli

One-carbon (C1) compounds, including carbon dioxide, carbon monoxide, formate, methanol, and methane, are attractive feedstocks for fuel and chemical production due to their availability and sustainability. However, the efficient and economical utilization of these feedstocks can be challenging for traditional chemical processes due, in part, to their diffuse nature. As a result, biological processes are gaining increased attention as alternatives due to safer, milder processing conditions and potential for scale-down, which may allow for decentralized, distributed chemical manufacturing that can make better use of these resources (Science 355, 38, 2017: doi: 10.1126/science.aag0804). In order for this potential to be realized, however, significant advances in the performance of C1-metabolizing enzymes, pathways and microorganisms must be achieved.

In this talk I will discuss our recent efforts to engineer and implement biological C1 utilization for chemical production. In one approach, we have leveraged the existing C1-utilization pathways of native methanotroph Methylomicrobium buryatense 5GB1 for the production of industrially relevant products such as lactate (JIMB 45:379, 2018). In an alternative approach, we engineered a synthetic metabolic pathway for C1 conversion to multi-carbon products that is distinctive from and orthogonal to any known metabolic network (Nat. Chem. Biol., 2019, MS in Revision). This C1 elongation pathway is enabled by our discovery that an enzyme involved in mammalian α-oxidation (2-hydroxyacyl-CoA lyase, HACL) can catalyze the condensation of formyl-CoA, an activated C1 molecule, with aldehydes of varying chain lengths. We have prototyped the pathway using a cell-free system with different C1 substrates and showed operation by synthesis of glycolaldehyde, glycolate, ethylene glycol, acetaldehyde, and lactate. We also demonstrated in vivo feasibility through the synthesis of glycolic acid and ethylene glycol by E. coli using formaldehyde as the sole carbon source. Our work establishes the potential for biotechnological applications of HACL, which includes both bioconversion of C1 feedstocks as well as synthetic methylotrophy and autotrophy.

Figure. Chemical production from C1 substrates using native and engineered methylotrophs