Omics-Driven Analysis of *Clostridium ljundhalii* Disentangles the Complexity of Energy Conservation Pathways at the Molecular Level

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Project goals: We aim to functionally annotate the *C. ljungdahlii* genome at ultra high resolution by integrating information from gene transcription, gene translation, transcription start sites and RNA polymerase binding sites. Furthermore, we reveal the translation efficiency in this model acetogen. We utilize the resulting knowledge to reconstruct a ME-model (*me*tabolic and gene-expression model). Finally, the optimized ME-model will guide strain design for production of valuable biocommodities and biofuels.

Acetogenesis is an integral part of the global carbon cycle and is driven by anaerobic bacteria that can fix CO_2 into acetyl-CoA and produce acetate as a by-product. *Clostridium ljungdahlii* is model homoacetogen of special interest due to its potential for production of fuels and other biocommodities from low-cost syngas (a mixture of CO_2, CO, and H_2). We developed novel omics techniques, including TSS-seq and Ribo-seq, to disentangle complex gene expression pattern at the levels of transcription and translation during growth under heterotrophic or autotrophic conditions.

We show that differentially translated genes in heterotrophic and autotrophic conditions are mainly involved in energy conservation and amino acid biosynthesis and import. Further, we show that some of these pathways are vastly regulated at the translational level. The amino acid biosynthetic pathways are differentially translated during heterotrophic growth, whereas during autotrophic growth these pathways are turned off and the oligopeptide permease is induced instead as a cost effective, but less effective source of amino acids.

Our omics-driven approach outlines the complex global regulation and gene architecture in *C. ljungdahlii* and provides valuable knowledge required for modeling, design and engineering of strains that are superior in renewable biofuels production.

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