A Metabolic and Gene-Expression Model Reveals New Insight Into the Acetogen *Clostridium ljungdahlii*

J. Liu[1]* (jkl055@ucsd.edu), A. Ebrahim[1], C. Lloyd[1], J. Kim[1], M.M. Al-Bassam[1], **K. Zengler**[1]

[1]University of California, San Diego, 9500 Gilman Drive 0419 La Jolla, CA 92093

http://sbrg.ucsd.edu

Project Goals: We have reconstructed a metabolic and gene-expression model (ME-model) for the acetogen *Clostridium ljungdhalii*. This model details the organism's interconnectivity of metabolism, energy conservation, and macromolecular synthesis in a computable format. We are now using the model to explore the potential for biocommodity production from inexpensive sources.

The acetogen *Clostridium ljungdahlii* has emerged as a potential chassis for strain designed chemical production for not only can it grow heterotrophically on a diverse set of sugars, but it can also grow autotrophically on carbon monoxide (CO), carbon dioxide (CO_2) and hydrogen (H_2), or a mixture of all three gases (i.e. syngas). When grown autotrophically, *C. ljungdahlii* metabolizes the gases into multi-carbon organics, an ability that can be redirected and engineered to produce biocommodities from low cost substrates.

To advance towards this goal, a constraint-based modelling method was used to systematize the biochemical, genetic, and genomic knowledge of *C. ljungdahlii* into a computable mathematical framework. This metabolic and gene expression model (ME-model) accounts for 961 ORFs that are responsible for the production of transcriptional units, functional RNAs (e.g., tRNAs, rRNAs), prosthetic groups, and cofactors as well as the formation and translocation of protein complexes. This macromolecular synthesis machinery (i.e. the E-matrix) enables the metabolic network (M-model). The two networks integrated together compute the molecular constitution of *C. ljungdahlii* as a function of genetic and environmental parameters. Furthermore, the ME-model predicts relative growth conditions that are conducive for secretion of products like acetate, ethanol, and more. For example, comparison to *in vivo* data allows us to hypothesize that batch grown *C. ljungdahlii* is capable of higher secretion rates if certain shifts in proteomic expression occur. With this ME-model, we have a foundation for predicting and understanding the phenotype of *C. ljungdahlii*, which is vital for effective strain design.

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