



Reconstructing the protein-protein interaction network of an industrial CO₂-assimilating anaerobe using comparative genomics and systematic literature curation

Vanessa Savvopoulou^{1,2#} and Maria I. Klapa^{1*}

¹ Metabolic Engineering & Systems Biology Laboratory, FORTH/ICE-HT, Patras, Greece

² Department of Chemistry, University of Patras, Greece

Presenting * Corresponding author, emails: vsavvop@iceht.forth.gr mklapa@iceht.forth.gr

ABSTRACT

Recently, there has been a surge of industrial interest in creating optimized engineering solutions for CO₂ capture and its conversion into biofuels and valuable chemicals. In light of this, research in non-photosynthetic CO₂ bioconversion has gained traction in metabolic engineering and industrial biotechnology, offering an alternative to traditional biomass-based microbial processes. However, the relevant microbial systems have not been extensively studied in the context of the new high-throughput biomolecular analyses. Multi-omic analyses are essential for enhancing our understanding of bacterial molecular physiology and regulation, insights valuable for guiding the metabolic engineering and biomanufacturing of these microbes. Acetogens, are the bacteria that can catabolize CO₂ through the Wood – Ljungdahl pathway under strictly anaerobic conditions; of this bacterial family, the thermophile obligatory anaerobe *Moorella thermoacetica* has been used as the model system due to its small fully-sequenced genome [1]. Due to its industrial interest, the metabolic network of the bacterium has been reconstructed and relevant metabolic boundaries have been determined. However, its protein-protein interaction (PPI) network remains unexplored. In general, PPI networks have not been extensively studied in bacteria. In this context, this study aimed at extending the biomolecular analysis toolbox of *M. thermoacetica* by reconstructing a high-confidence experimentally-supported PPI network.

Using strict criteria for inclusion of experimentally-supported data, we identified a network of 86 PPIs between 67 proteins, based on a very limited number of experimentally-detected PPIs in *M. thermoacetica*, augmented by data from systematic literature curation, comparative genomics with experimentally-detected direct PPI networks of *Bacillus subtilis* and *Escherichia coli*, and the highly-scored experimentally-supported protein associations listed in STRING database (<https://string-db.org/>) [3]. The acquired results support the need to pay close attention to the elucidation of microbial PPI networks, especially of the extremophiles that have gained industrial interest, because they provide valuable insights and new directions for physiological characterization experiments that are currently lacking in the literature. It is important to bridge the biomanufacturing with the molecular biology and omic analysis fields.

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