Company Name: Lygos Inc.
Project Title: Accelerating engineered microbe optimization through machine learning and multi-omics datasets
Principle Investigator: Dr. Jeffrey Dietrich

Currently the US chemicals industry is near completely dependent on petroleum and natural gas feedstocks. Steadily rising petroleum feedstock prices – a trend predicted to continue into the foreseeable future – and increased price volatilities are decreasing U.S. competitiveness in industrial chemical manufacturing. In 1995, the U.S. exhibited a trade surplus of $20B in industrial chemicals; the U.S. now runs a deficit. It would be advantageous to the U.S. economy to develop novel routes to existing chemicals based on renewable feedstocks.

Lygos is addressing this problem by developing microbial catalysts to convert renewable cellulosic sugars into higher-value commodity and specialty chemicals. Lygos is a part of the overall strategy to replace the whole barrel of oil and specifically targets "bio-advantaged chemicals," compounds that are expensive to make petrochemically and can be produced biologically for less than the petrochemical raw material cost. These are chemicals where the market size is constrained by production cost and a lower-cost, biological process can enable market growth.

The objective of this project is to implement a high-throughput microbial engineering Design-Build-Test-Learn cycle incorporating transcriptomic, metabolomic, and proteomic analyses along with machine learning. These technologies have the potential to both accelerate and decrease the cost to optimize small-molecule production in microbial hosts. Furthermore, they are particularly well-suited for use with non-traditional microbes that are not well characterized. In collaboration with the Agile BioFoundry, Lygos will implement this high-throughput DBTL workflow to improve production of the target biochemical in *Pichia kudriavzevii*, an acid tolerant strain of yeast. Planned strain improvements include overexpression of pathway proteins and reduction or deletion of native yeast metabolic genes and pathways. The performance of the engineered strain in fermentation will be assayed using cellulosic sugar as a raw material.

The outcome of successful project completion includes a cost-advantaged process to a high-value biochemical. Commercialization of the technology as a bolt on plant in an integrated biofuels biorefinery also helps to improve integrated biorefinery economics, driving biofuel production cost to below $3/gallon gasoline equivalent and 50% reduction in GHG emissions.