## 212. A functional genomics approach to improving microbial fermentation

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**Project Goals**
Efficient and sustainable conversion of cellulosic derived sugars to biofuel is dependent on robust microbial fermentation. Fermentation stressors, such as lignocellulosic derived inhibitors, are major hurtles to conversion of sugars. Further, the limited ability of powerful ethanologens like the yeast *Saccharomyces cerevisiae* to convert xylose to ethanol impedes potential yields. To improve biofuel productions, at the DOE Great Lakes Bioenergy Research Center we are using Systems Biology to overcome these roadblocks to create superior biocatalysts

**Abstract**
In addition to its role as the primary industrial ethanol producing microbe, the yeast *Saccharomyces cerevisiae* is powerful tool for genetics and as such benefits from a suite of systems biology tools, which can be leveraged to improve biofuel production. We have developed new reagent sets for understanding the roadblocks to efficient bioethanol production. Using yeast chemical genomics, we have developed a high-throughput, low-cost method of "biological fingerprinting" lignocellulosic hydrolysates that can be used to identify nutrient limitations as well as lignocellulosic derived inhibitors (LCDIs). Further, through chemical genomic analysis of a novel LCDI we have determined the mode-of-action of an uncharacterized compound that exerts toxicity by attacking the yeast cell wall, and has potential as a value-added bioproduct from cellulosic hydrolysates. Additionally, we have transformed industrially-relevant, xylose-fermenting yeast with a genome-wide, barcoded ORFeome collection (MoBY-ORF 2.0) to allow massively-parallel, gain-of-function studies and chemical genetic interactions. With this system we have identified genes that confer specific tolerance to anaerobic hydrolysate fermentation. These data will serve as the basis for rational engineering of yeast for bioconversion of next-generation biofuels.

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