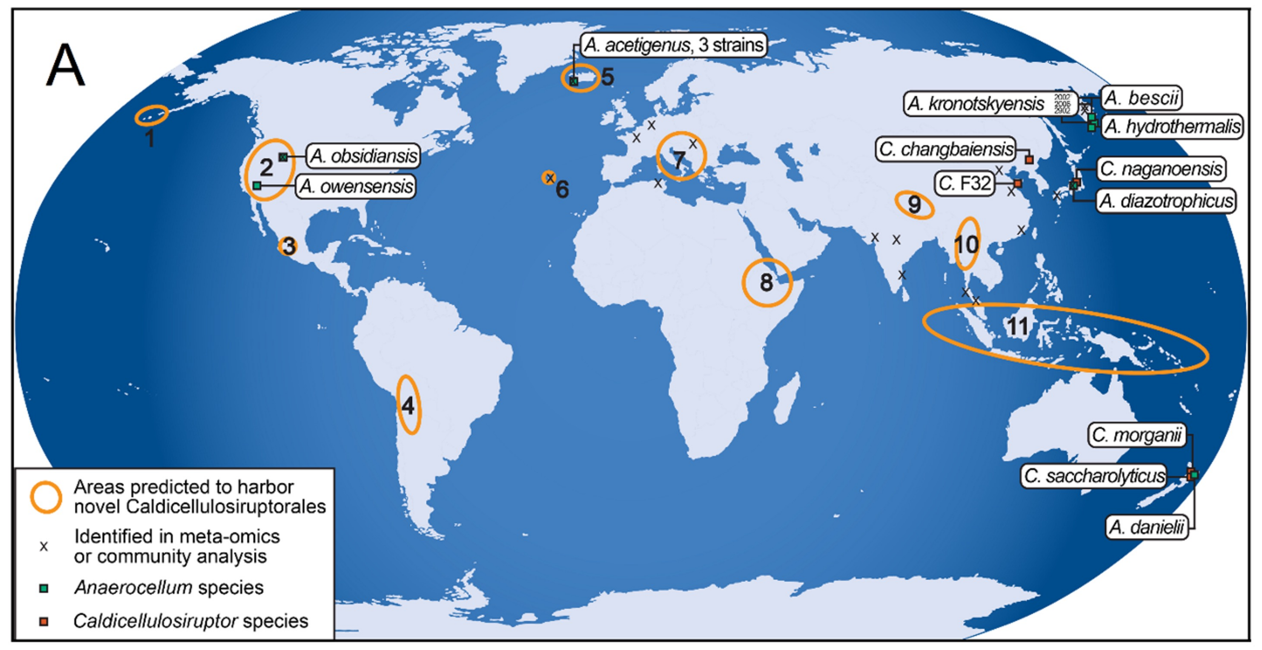
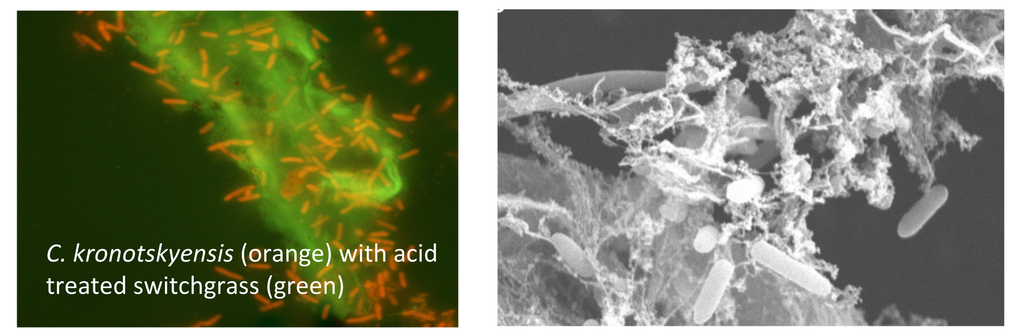
Kelly Lab: Hyperthermophile Biology and Biotechnology

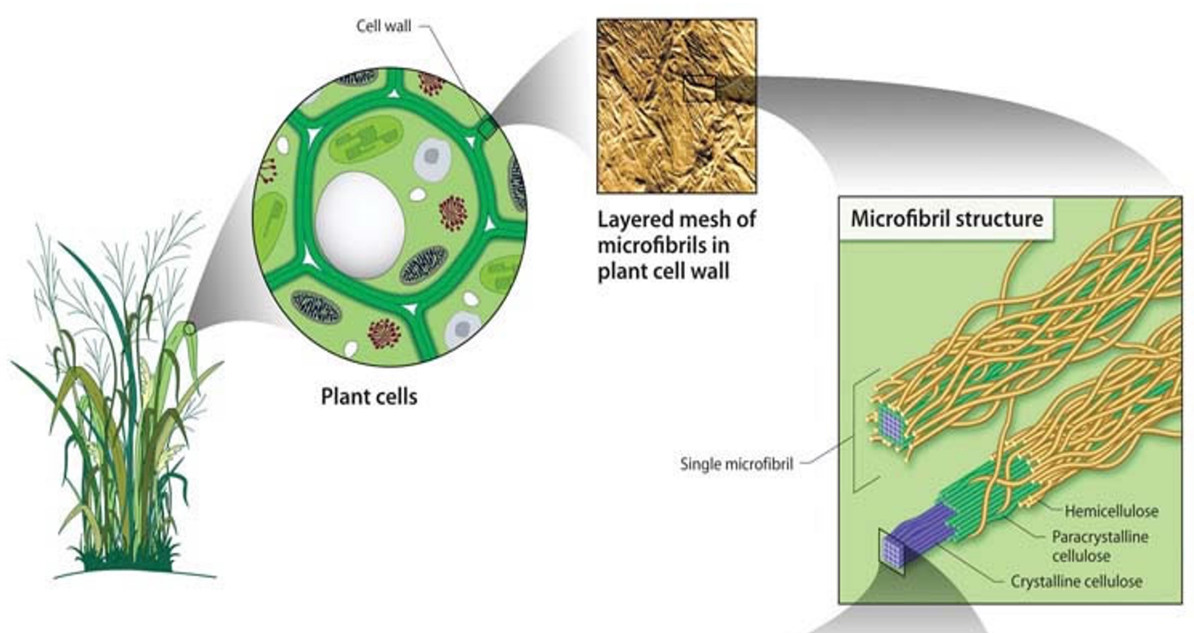
Lignocellulose Conversion to Bio-based Chemicals

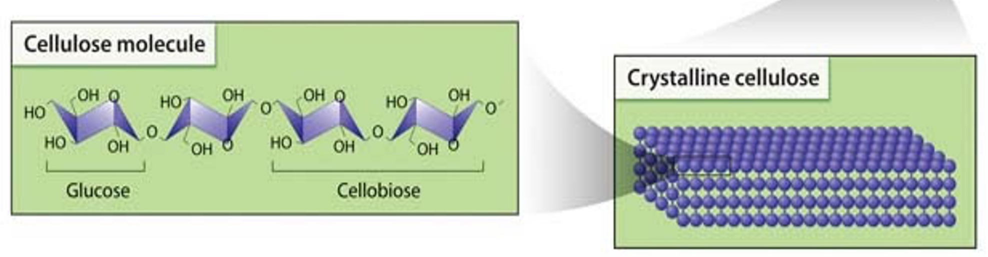


Caldi cells growing on plant biomass



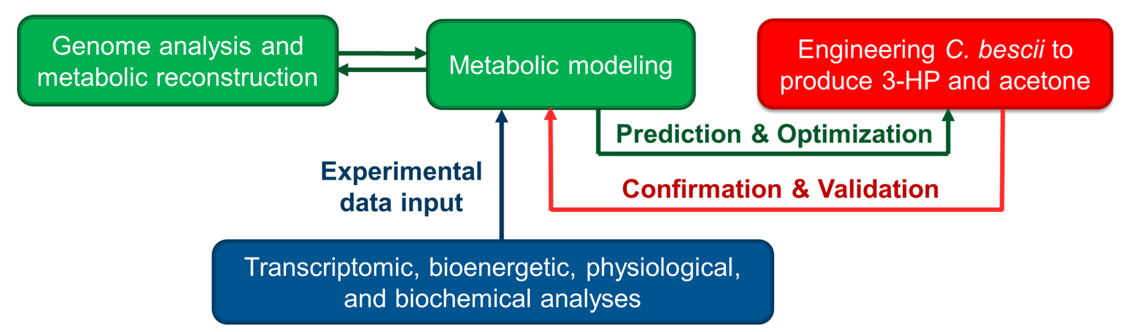
Caldicellulosiruptoraceae are found globally, and have various abilities to degrade and metabolize plant biomasses



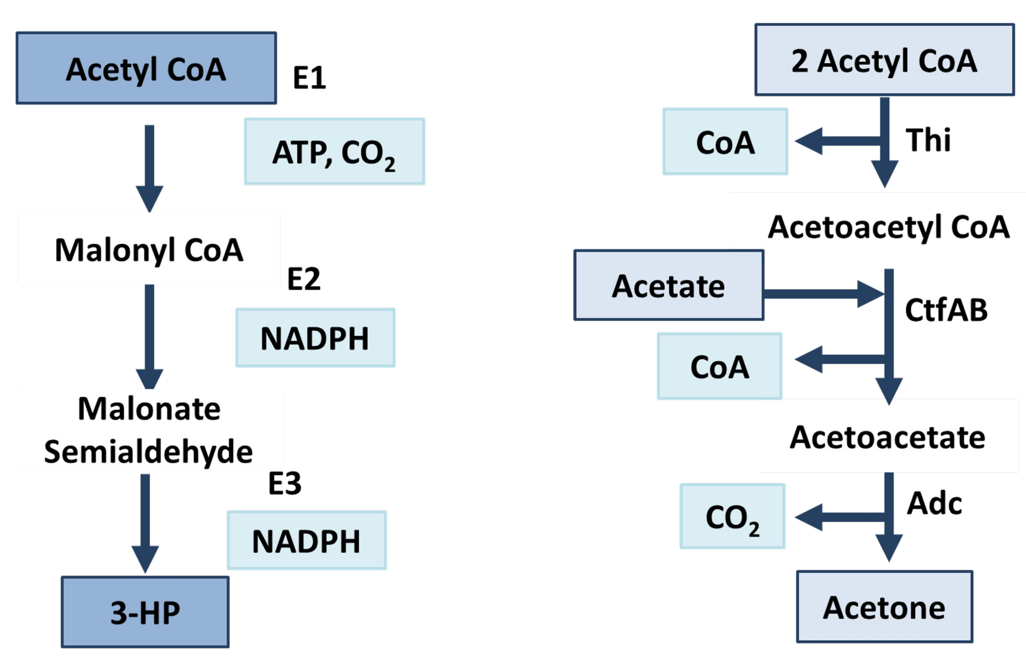


Caldi species use different strategies to interact with lignocellulose carbohydrates, including microcrystalline cellulose. More importantly, Caldi species also have an ability to degrade unpretreated plant biomass. Therefore, Caldi species are promising candidates for Consolidated BioProcessing, which requires the microorganism that has ability to hydrolyze unpretreated plant biomass and convert it into valuable chemicals, all in the same microorganism.

Metabolic Engineering of *A. bescii* for Industrial Chemical Production

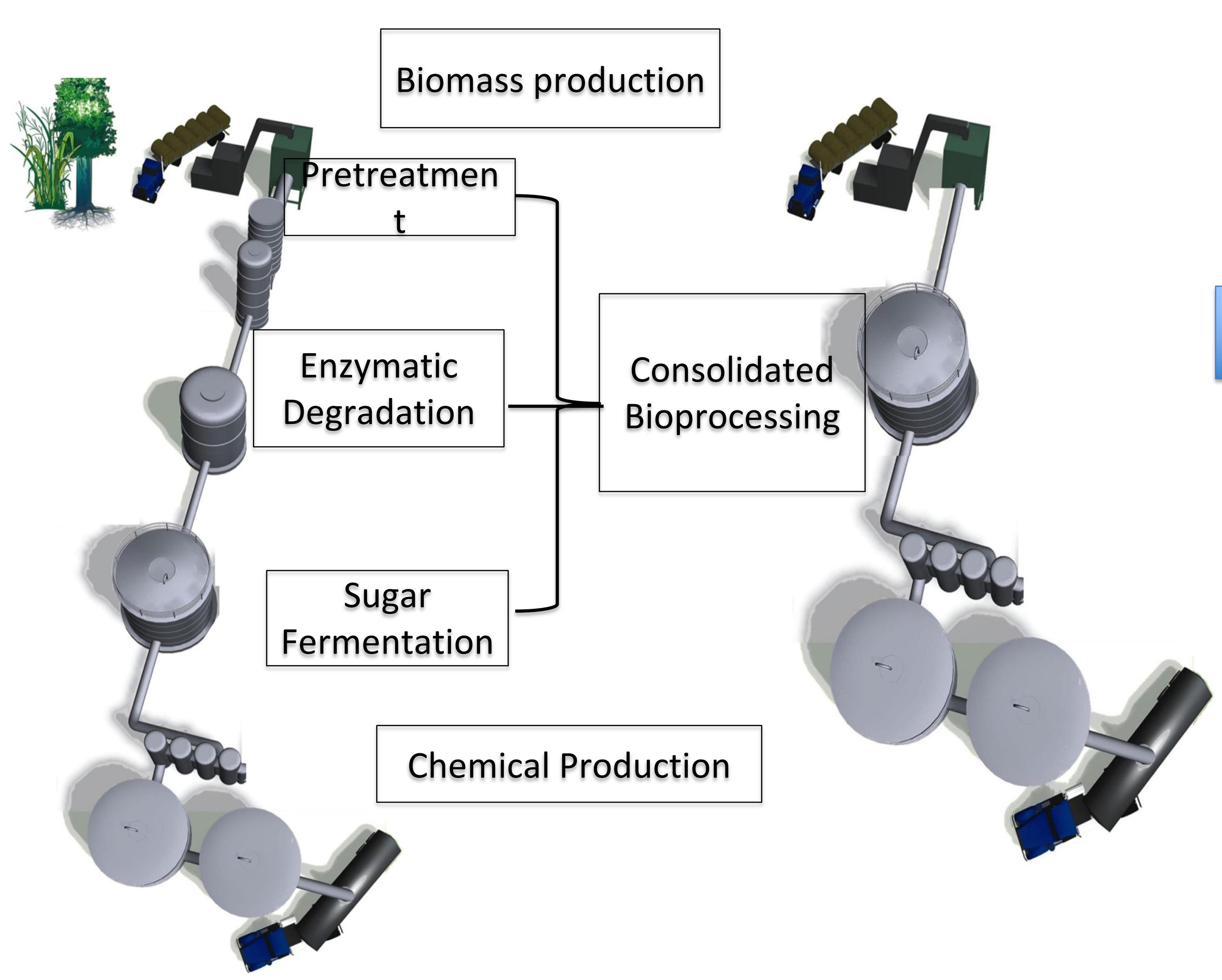


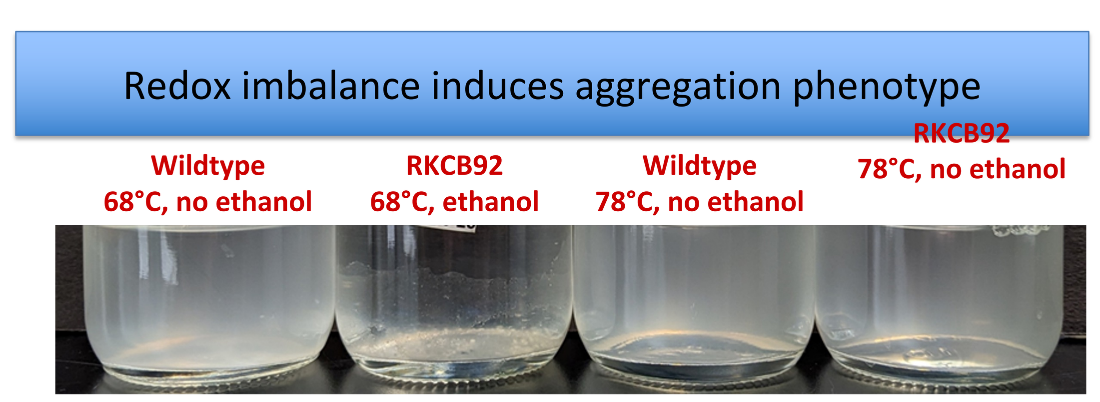
Goal: Generate engineered strains of *A. bescii* optimized for conversion of lignocellulose through model guided metabolic engineering. Target products include acetone and 3-hydroxypropionate, as well as ethanol, succinate, propanol



Increasing product titer and selectivity by rewiring *A. bescii* metabolism

Goal: Produce commodity chemicals at industrially relevant levels and selectivities. Use ethanol producing strains to prove metabolism can be redirected to a non-native product.





Current progress:

- Achieved up to 80% selectivity to ethanol
- Increased titers, work still in progress
- Redox imbalance (NAD(P)H, ferredoxin) causes aggregation phenotype. In ethanol stains, high selectivity is associated with aggregation and filming

Extreme Thermoacidophiles

Found in acidic hot springs and solfatara world-wide:

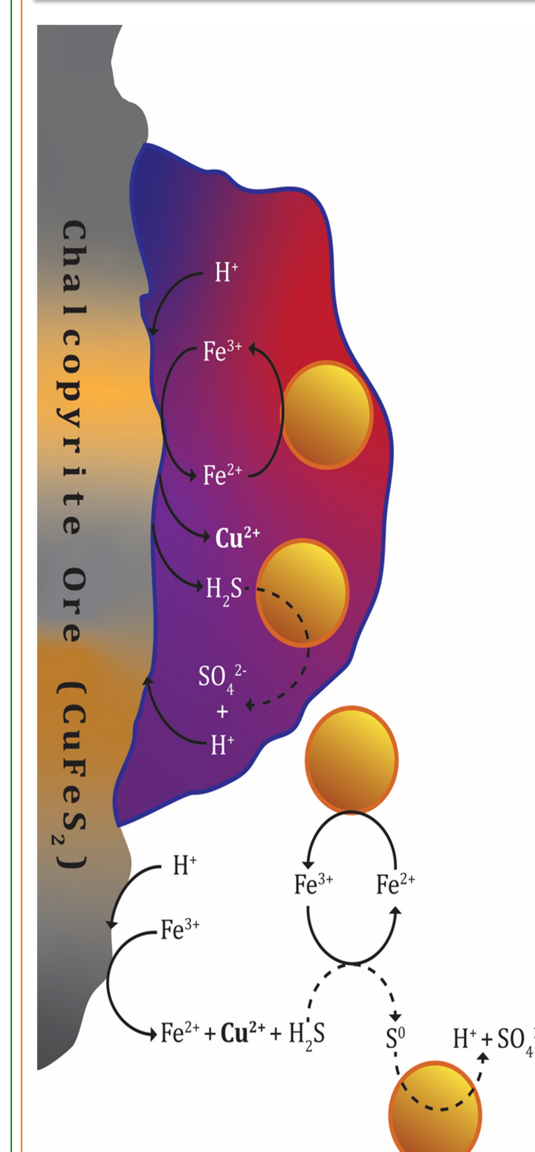
- Extremely Thermophilic (>65 ˚C)
- Acidophilic (pH <4)

Varied Metabolisms:

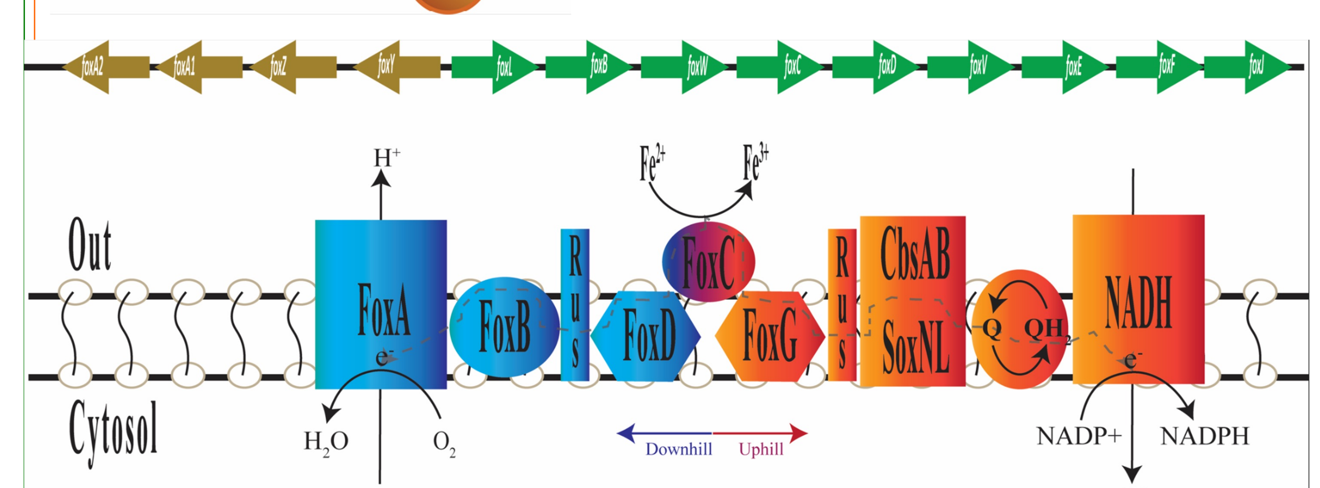
- Iron oxidation/reduction
- Sulfur oxidation/reduction
- Carbon assimilation via CO_2
- Heterotrophy

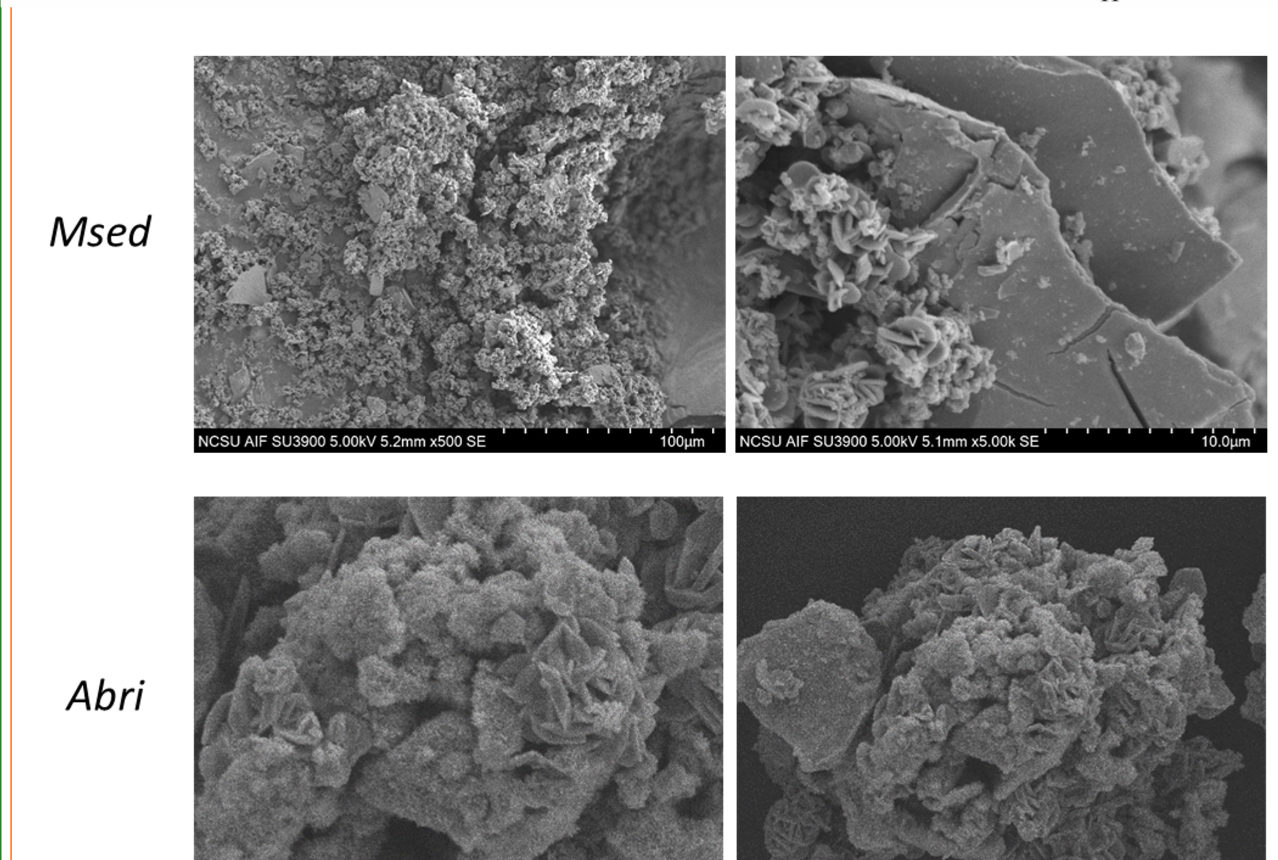
Research conducted under Yellowstone Research Permit YELL-2023-SCI-8304

Bioleaching with Thermoacidophiles

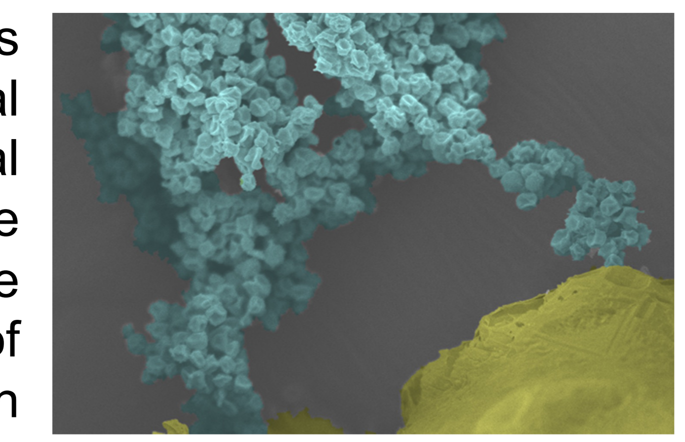


One of the main disadvantages of traditional methods of metal mining is the environmental impacts. Novel technologies are needed to decrease environmental side effects of metal extraction from ores. In this case, bioleaching, the process of extracting metals using microorganisms, has been explored as one of the better alternatives to traditional metal ore extractions. Thermoacidophiles, including *Acidianus brierleyi* (*Abri*), and *Metallosphaera sedula* (*Msed*), have been explored due to their ability in sulfur and iron oxidation.





Building a Chemolithoautotroph



Thermoacidophiles use the energy from biooxidation to power CO_2 fixation, creating an opportunity to product industrially relevant organic chemicals from inorganic carbon.

Sulfolobus acidocaldarius **(*Saci*)** is a genetically tractable species of thermoacidophile that has lost the ability to oxidize sulfur. We use comparative phenotyping and multi-omics to uncover the metabolic pathways of biooxidation. We use these findings to genetically engineer and model *Saci* to support chemolithoautotrophy that produces industrially relevant organic chemicals.